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THE NITRATION OF 2-NITRAMINOTHIAZOLES AND 2-ACETAMIDOTHIAZOLES¹

BY SILVIO J. VIRON² AND ALFRED TAURINS

ABSTRACT

It has been shown by nitration with a mixture of 99-100% nitric acid and acetic anhydride that 2-nitraminothiazoles, such as 2-nitramino-5-nitrothiazole and 4-methyl-2-nitramino-5-nitrothiazole, can react in the tautomeric nitrimino form. The nitration occurs in the three position of the thiazole ring. Compounds with an acetamido group in the two position of the thiazole ring, such as 2-acetamido-5-bromo-2-thiazole and 2-acetamido-5-methylthiazole, can also be nitrated in the three position indicating the tautomeric change from the acetamido to the acetimido group.

INTRODUCTION

Studies on nitration of 2-amino- and 2-acetamidothiazoles have been reported by several authors. Babo and Prijs (1) investigated the nitration of 2-aminothiazole. If the reaction is allowed to proceed for 12 hr., the nitration occurs in the amino group as well as in the five position, giving 2-nitramino-5-nitrothiazole (I).

Ochiai and Nagasawa (10) reported the nitration of 2-amino-4-methylthiazole which was prepared by the method of Dodson and King (3) to 4-methyl-2-nitramino-5-nitrothiazole (II). Nagasawa (9) prepared 2-amino-5-methylthiazole from 2-bromopropionaldehyde diethyl acetal and thiourea. An attempted nitration of this compound was unsuccessful. The nitration of 2-acetamido-5-methylthiazole (IV) gave a small yield of 2-acetamido-5-methyl-4-nitrothiazole.

The nitration of 2-acetamidothiazole was described by Ganapathi and Venkantaraman (5) who used a mixture of sulphuric and nitric acid at 10° to obtain 2-acetamido-5-nitrothiazole (V). The hydrolysis of (V) gave 2-amino-5-nitrothiazole, which could be also obtained by the nitration of 2-aminothiazole at low temperature.

Bellavita (2) showed that ethyl nitrate could be used as a nitrating agent for these compounds. Both 2-aminothiazole and 2-amino-4-methylthiazole

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Contribution from the Organic Chemistry Laboratory, McGill University, Montreal, Que., with the financial assistance of the National Research Council of Canada, Ottawa.

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² Holder of a National Research Council Studentship 1951-1952.

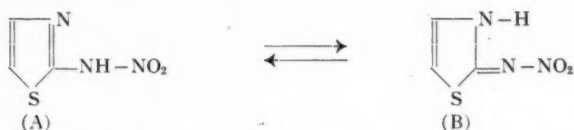
were nitrated in the five position to give 2-amino-5-nitrothiazole and 2-amino-4-methyl-5-nitrothiazole.

The same author found that nitration of 2-acetamidothiazole and 2-acetamido-4-methylthiazole with ethyl nitrate gave 2-acetamido-5-nitro derivatives. The nitration of 2-acetamido-5-bromothiazole (III) resulted in the replacement of halogen by a nitro group as it was observed by Hurd and Wehrmeister (7) who obtained 2-acetamido-5-nitrothiazole. Similar replacement of bromine atoms by nitro groups has been observed in thiophene series (6).

The objective of this work was to study the further nitration of 2-nitramino-5-nitrothiazoles to obtain evidence of the existence of the tautomeric nitrimino forms of these compounds. Similarly, the nitration of 2-acetamidothiazoles was studied to prove the existence of the tautomeric acetimido forms.

DISCUSSION

The structure of 2-nitraminothiazole can be visualized in two tautomeric nitramino (A) and nitrimino (B) forms.



Similarly, 2-acetamidothiazole can undergo the tautomeric change between acetamido (C) and acetimido (D) structures.



The nitration of these compounds can occur in the position three only if the entering nitro group replaces the hydrogen atom which is attached to the ring nitrogen atom in the indicated position, in other words, if these compounds react in their nitrimino or acetimido forms.

Nitration of 2-Nitraminothiazoles

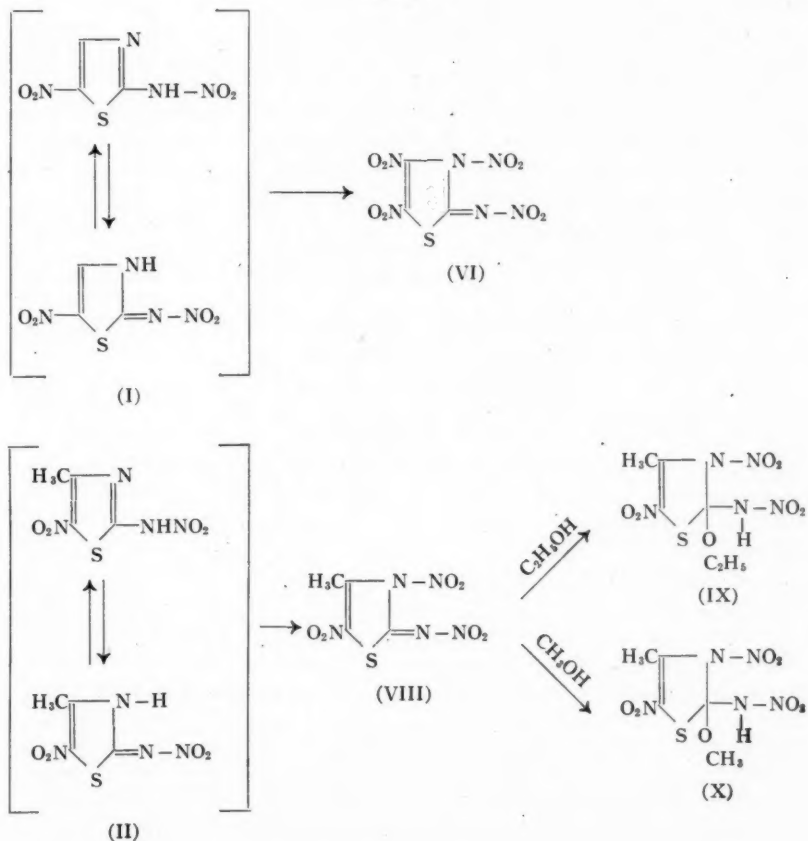
The nitration was carried out with a mixture of 99–100% nitric acid and acetic anhydride at temperatures between 0 and 5°. The original compounds (I) and (II) dissolved in the nitration mixture and new compounds precipitated after a short time.

The isolation of the reaction product met with some difficulties. If the nitration product from (I) was allowed to stand after filtration without removal of the acid by washing it turned rather gummy in approximately fifteen minutes and then exploded. The best results were obtained if the product was washed well with glacial acetic acid. The recrystallization from benzene gave white crystals melting at 121–123°. Analysis of the nitration product

indicated that it contained three nitro groups in the thiazole ring, and could be named as 2-nitramino-3,4,5-trinitro-2-thiazolone (VI). It seems that the unusually high accumulation of nitro groups in (VI) is responsible for its instability. Attempts to prepare derivative with alcohol failed, because the product was an oil which decomposed readily. The compound (VI) was obtained by another method, namely, the nitration of 3,4-dinitro-2-thiazolimine, which will be discussed later.

The nitration product from (II) had better properties. After filtration, washing with glacial acetic acid, and drying, the new product melted at 89° with decomposition. Attempts to recrystallize this compound from benzene, ethyl acetate, or nitromethane failed owing to the decomposition. When the product was added to ethyl alcohol, it went into solution immediately. The addition of water precipitated a compound melting at 136° with decomposition. This product could be recrystallized from benzene or by solution in ethyl

CHART I



alcohol, filtration, and precipitation by the addition of water. The analysis of this compound conformed to the structure for 3,5-dinitro-2-ethoxy-4-methyl-2-nitramino- Δ^4 -thiazoline (IX). It has been concluded that the original nitrated compound was 3,5-dinitro-4-methyl-2-nitrimino-2-thiazolone (VIII), which has added a molecule of ethanol to form (IX). The similar addition was found to occur when methanol was used in place of ethanol. The methanol derivative had a melting point 132°. It could be recrystallized from benzene or by solution in methanol followed by reprecipitation with water. The analytical data fitted the structure for 3,5-dinitro-2-methoxy-4-methyl-2-nitramino- Δ^4 -thiazoline (X).

The foregoing results are similar to those obtained by McKay and Wright (8) for the reaction of alcohols on 1-nitro-2-nitramino- Δ^2 -imidazoline to form 2-alkoxy-2-nitramino-1-nitro- Δ^2 -imidazoline.

The procedure of Babo and Prijs (1) for nitration of 2-aminothiazole to 2-nitramino-5-nitrothiazole was found unsatisfactory, since the step involving the pouring of the reaction mixture onto ice causes partial decomposition. The yield of (I) was greatly improved and a purer product obtained if the excess nitric acid was decomposed by the careful addition of absolute ethanol until gassing had ceased. Extreme caution must be observed in the addition of alcohol. If the alcohol is added too quickly or the temperature is allowed to rise above 40°, the mixture may froth over. After the excess acid had been decomposed, the mixture was poured onto crushed ice with the separation of a good yield of almost pure 2-nitramino-5-nitrothiazole.

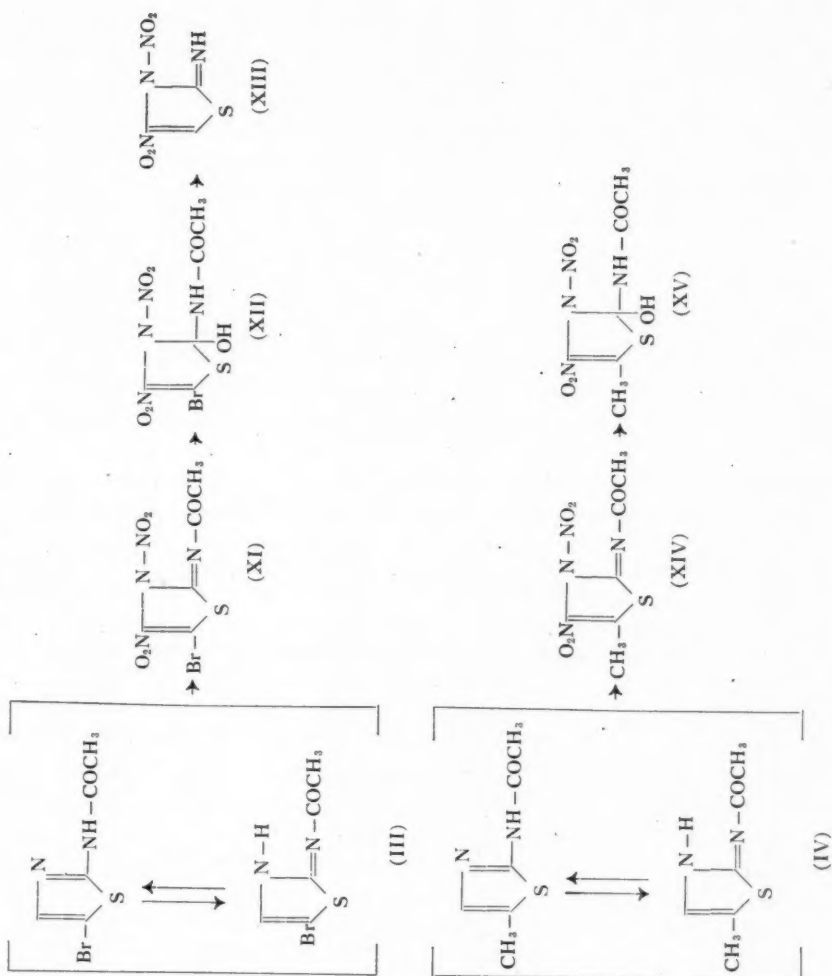
Nitration of 2-Acetamidothiazoles

We nitrated 2-acetamido-5-bromothiazole with a mixture of 99–100% nitric acid and acetic anhydride.

2-Acetamido-5-bromothiazole (III) was prepared by first brominating 2-aminothiazole in glacial acetic acid followed by the acetylation of acetic anhydride of the compound obtained as described by Erlenmeyer and Kiefer (4). The nitration of (III) with 99–100% nitric acid in acetic anhydride yielded a compound which after the filtration must be washed well with glacial acetic acid to prevent the decomposition. After isolation the product was dried in a vacuum desiccator. Recrystallization of this compound from benzene yielded white needle-like crystals, which melted at 119–120°. The analysis of the substance conformed to the structure of 2-acetamido-5-bromo-3,4-dinitro-2-hydroxy- Δ^4 -thiazoline (XII) which was preceded by the intermediate 2-acetamido-5-bromo-3,4-dinitro-2-thiazoline (XI). In this nitration reaction the bromine atom was not replaced as has been observed in other similar cases. Thus Hurd and Priestley (6) reported that red fuming nitric acid and acetic anhydride replaced the bromine atoms in 2-acetamido-3,5-dibromothiophene.

(XII) was easily hydrolyzed by boiling water. It was refluxed with water until complete solution, filtered hot, and then allowed to cool. As the solution cooled it deposited long yellow needles. This compound after recrystallization from water had a melting point of 172° (exploded), showed a negative test for bromine, and analyzed for 3,4-dinitro-2-thiazolinimine (XIII).

CHART II



The nitration of 3,4-dinitro-2-thiazolinimine in 99–100% nitric acid and acetic anhydride yielded (VI), m.p. 121–122°, recrystallized from benzene. A mixed melting point with a sample of (VI) obtained by nitration of 2-nitramino-5-nitrothiazole showed no depression. The compound was easily decomposed by water and alcohol.

2-Amino-5-methylthiazole was prepared according to Nagasawa (9) and acetylated with acetic anhydride to obtain 2-acetamido-5-methylthiazole (IV). The reaction of (IV) with 99–100% nitric acid and acetic anhydride was allowed to proceed for 20 hr. at room temperature. The mixture was then poured onto crushed ice with the separation of a viscous substance. After decantation of the solution followed by trituration of the viscous produce with ethanol, a crystalline compound was obtained. It was recrystallized from ethyl acetate and benzene, and obtained in white crystals, m.p. 151.5–152°. The analysis conformed to the structure for 2-acetamido-3,4-dinitro-2-hydroxy-5-methyl- Δ^4 -thiazoline (XV). It is very probable that it was formed by the addition of a molecule of water to the nitration product (XIV).

The nitration of 2-acetamidothiazole with 99–100% nitric acid and acetic anhydride under the conditions described for (III) gave the same product 2-acetamido-5-nitrothiazole, m.p. 264–265°, as obtained by nitration of 2-acetamidothiazole with a nitric-sulphuric acid mixture (5).

EXPERIMENTAL

Preparation of 2-Nitramino-5-nitrothiazole (I)

A solution of 10 gm. of 2-aminothiazole in 7 ml. of concentrated sulphuric acid was added to a mixture of 14 ml. of 90–95% nitric acid and 7 ml. of concentrated sulphuric acid with stirring at the temperature of 0–5°. The reaction mixture was stirred for two hours at this temperature range. Absolute alcohol was added drop by drop to decompose the excess nitric acid. Extreme care must be taken during this addition. The temperature must not be allowed to rise above 20 and the ethyl alcohol must not be added too quickly, otherwise the mixture may froth over. The ethanol was added until no further gassing was observed and then the mixture was poured onto 25 gm. of crushed ice. In this manner 9.1 gm. of almost pure 2-nitramino-5-nitrothiazole was obtained, melting at 167° (exploded).

Nitration of 2-Nitramino-5-nitrothiazole (I)

The following procedure was used for nitration of 2-nitraminothiazoles and 2-acetamidothiazoles.

Seven milliliters of acetic anhydride were added dropwise with stirring at 5° to 3 ml. of 99–100% nitric acid contained in a 125 ml. three-necked flask provided with a thermometer, mechanical stirrer, and dropping funnel. To this nitration mixture 5 gm. of (I) were added portionwise with stirring at such a rate that the temperature remained below 5°. The solid dissolved in approximately five minutes and after 30 min. the mixture started to become turbid. In a few minutes the mixture became semisolid.

Five milliliters of glacial acetic acid was added to make the mixture more

fluid and stirring continued for an additional two hours. The mixture was then filtered and the product washed well with glacial acetic acid. The white crude product after drying weighed 5.45 gm. It could be recrystallized from either glacial acetic acid or benzene to obtain white crystals of (VI) melting at 121–123° (decomp.). The crystals decomposed slightly on longer standing with evolution of brown nitrogen dioxide.

Anal. calc. for $C_3N_6O_8S$: C, 12.87%.

Found: C, 12.68%.

Preparation of 4-Methyl-2-nitramino-5-nitrothiazole (II)

Five grams of 2-amino-4-methylthiazole was dissolved in 7 ml. of concentrated sulphuric acid, with cooling, and this solution added slowly to the nitrating mixture (at 5°) consisting of 7 ml. of fuming nitric acid and 7 ml. of concentrated sulphuric acid. Stirring was continued for an additional four hours after complete addition. The excess nitric acid was decomposed by slow addition of absolute alcohol below 20° and the mixture was poured onto 20 gm. of crushed ice; 4.8 gm. (69.0%) of 4-methyl-2-nitramino-5-nitrothiazole was obtained. The substance was recrystallized from glacial acetic acid and obtained in the form of yellow plates; m.p. 184–185° (decomposition). The reported melting point of (II) is 185° (10).

Nitration of 4-Methyl-2-nitramino-5-nitrothiazole (II)

To a nitrating mixture consisting of 1.5 ml. of 99–100% nitric acid and 3.5 ml. of acetic anhydride, 5 gm. of (II) was added portionwise with stirring at 5°. The mixture was stirred for two hours at this temperature. During this time the original had dissolved and a new product precipitated. Three milliliters of glacial acetic acid was added to facilitate stirring and the temperature was allowed to rise to 20°. The reaction mixture was allowed to stand without stirring for 10 hr. at room temperature. The white solid product (VIII) was collected on a filter, dried, and weighed (2.1 gm.); m.p. 98° (exploded). Many attempts to purify this substance were unsuccessful. When the nitrocompound was warmed with solvents such as benzene, ethyl acetate, or glacial acetic acid, brown fumes of nitrogen dioxide were liberated.

(a) Ethanol Derivative of the Nitration Product:

3,5-Dinitro-2-ethoxy-4-methyl-2-nitramino- Δ^4 -thiazoline (IX)

A portion of the nitration product (VIII) was dissolved in ethanol. Water was added to the solution to precipitate a white solid. After two recrystallizations from ethanol and the addition of water, it melted at 141–142° with gassing.

Anal. calc. for $C_6H_9N_5O_7S$: C, 24.39; H, 3.05%.

Found: C, 24.52; H, 3.11%.

(b) Methanol Derivative of the Nitration Product:

3,5-Dinitro-2-methoxy-4-methyl-2-nitramino- Δ^4 -thiazoline (X)

In a similar manner a new product was obtained by dissolving (VIII) in methanol and precipitating with water. Two recrystallizations from methanol

by addition of water gave a product melting at 133–134°, with gassing.

Anal. calc. for $C_8H_7N_3O_7S$: C, 21.36; H, 2.84%.

Found: C, 21.50; H, 3.03%.

Preparation of 2-Acetamido-5-methylthiazole (IV)

Four grams of 2-amino-5-methylthiazole (9) was dissolved in 25 ml. of glacial acetic acid and 10 ml. of acetic anhydride. After the mixture had stood for two hours crystals started to separate. The mixture was allowed to stand for five hours, and then diluted with 50 ml. of water with the separation of 5.2 gm. (94%) of 2-acetamido-5-methylthiazole, m.p. 225°.

Nitration of 2-Acetamido-5-methylthiazole (IV)

Five grams of (IV) were nitrated with a mixture of 5.3 ml. of 99–100% nitric acid and 13 ml. of acetic anhydride at 0–5°. The mixture was allowed to stand at room temperature for 20 hr., and then poured onto 10 gm. of crushed ice with a separation of viscous substance. After trituration of the gummy mass with 2 ml. of ethanol a crystalline product was formed (1.4 gm.; 13%). Recrystallization was effected by dissolving the product in warm ethyl acetate, filtering it, and adding benzene. The substance (XV) melted at 151.5–152°.

Anal. calc. for $C_8H_8N_4O_6S$: C, 27.27; H, 3.03; N, 21.21%.

Found: C, 27.59; H, 2.99; N, 21.03%.

Nitration of 2-Acetamido-5-bromothiazole (III)

Five grams of (III) were nitrated with a mixture of 5.5 ml. of 99–100% nitric acid and 13.2 ml. of acetic anhydride at 0–5°. The solid dissolved in a few minutes and after 10 min. a new product precipitated. Five milliliters of glacial acetic acid was added to make the mixture more fluid. It was allowed to stand for two hours at 20°. The product was filtered, washed with glacial acetic acid, and pressed as dry as possible. The yield was 3.7 gm. Two recrystallizations from benzene yielded white needlelike crystals (XII), m.p. 119–120°.

Anal. calc. for $C_6H_5N_4O_6BrS$: H, 1.22; N, 17.02%.

Found: H, 1.58; N, 16.58%.

3,5-Dinitro-2-thiazolinimine (XIII)

One gram of (XII) was added to 5 ml. of water and the mixture refluxed for 30 min. During this period the solid dissolved and the solution took on a distinct yellow color. The solution was filtered hot and allowed to cool. While cooling, the solution deposited long needlelike crystals weighing 0.6 gm. Some of these crystals were as long as 2 cm. in length. The product melted at 172° (exploded) and the melting point did not change after one recrystallization. The same compound could be obtained by refluxing the original nitrated product with either ethanol or *n*-propanol.

Anal. calc. for $C_3H_2N_4O_4S$: C, 18.95; H, 1.05; N, 29.46%.

Found: C, 19.20; H, 1.69; N, 29.46%.

Nitration of 3,5-Dinitro-2-thiazolinimine (XIII)

To 0.6 ml. of nitric acid (99–100%) contained in a test tube, cooled to 0°, was added dropwise 1.5 ml. of acetic anhydride. To the nitrating mixture,

1.0 gm. of (XIII) was added at such a rate that the temperature did not rise above 5° while the mixture was being cooled in an ice-salt bath. On being shaken, the solid dissolved slowly. The mixture was then allowed to stand for two hours at 0° with occasional shaking. After this time crystals had separated which after filtration and drying weighed 0.6 gm. After two recrystallizations from benzene, the substance melted at 123° (decomposition).

The product appeared to be the same as the compound (VI) obtained from the nitration of 2-nitramino-5-nitrothiazole (I). The compound was decomposed by water and alcohols, and produced a deep red coloration with alkalis. A mixed melting point with a sample of (VI) obtained by nitration of (I) showed no depression.

2-Acetamido-5-nitrothiazole

Four grams of 2-acetamidothiazole was nitrated with a mixture of 2.2 ml. nitric acid (99–100%) and 5.3 ml. acetic anhydride with constant stirring at 0–5°. After complete addition, the mixture was allowed to stand for five hours at 20°, during which time the product had separated. The product was collected on a filter and dried. The weight of crude 2-acetamido-5-nitrothiazole was 1.6 gm., melting at 264–265°. The filtrate was poured onto 10 gm. of crushed ice with the separation of more of the nitration product, weighing 0.8 gm. The over-all yield of it was 2.4 gm. (45.5%).

ACKNOWLEDGMENT

The analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.

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THE ALKALOIDS OF *LYCOPODIUM* SPECIES

XIII. *LYCOPODIUM DENSUM* LABILL.¹

By R. H. F. MANSKE

ABSTRACT

Lycopodium densum has yielded lycopodine and two apparently new alkaloids, L34, $C_{16}H_{25}O_2N$, and L35, $C_{14}H_{21}ON$. The total alkaloid content of the plant was less than 0.1%.

The alkaloid lycopodine has always been observed as one of the constituents of *Lycopodium* from the northern hemisphere but thus far it has not been isolated from a *Lycopodium* of southern origin (2). It is of course unlikely that the geographic distribution of these plants is a major factor in determining their alkaloid content. An examination of *Lycopodium densum* Labill. of New Zealand origin has now disclosed the presence of lycopodine and two other alkaloids, L34, $C_{16}H_{25}O_2N$, and L35, $C_{14}H_{21}ON$. Undoubtedly other alkaloids are elaborated by this plant but since the total alkaloid content was only 0.07% there was inadequate material for a more complete examination. Nicotine was not detected.

EXPERIMENTAL

The dried plant material which weighed 2365 gm. was received from Dr. L. B. Moore, Botany Division, Department of Scientific and Industrial Research, Wellington, New Zealand.

Alkaloid L34

The crude alkaloid (1) was subjected to slow distillation from a bulb tube in an air oven. Only two distinct fractions were obtained,—120–135° at 0.3 mm. and 165–170° at 0.3 mm.

The second fraction crystallized with great facility. It was washed with ether, dissolved in a large volume of boiling acetone, the solution concentrated to a small volume, and then treated with ether. The stout, well developed prisms of alkaloid L34 which then separated melted sharply at 236°. Found: C, 72.62; H, 9.25; N, 4.99%. Calc. for $C_{16}H_{25}O_2N$: C, 73.00; H, 9.51; N, 5.32%.

Alkaloid L35

The fraction of lower boiling point which was partly crystalline was washed with ether and recrystallized twice from the same solvent. Alkaloid L35 thus obtained consisted of stout, colorless polyhedra which melted at 133°. Found: C, 76.58, 76.46; H, 9.82, 9.84; N, 6.00, 5.74%. Calc. for $C_{14}H_{21}ON$: C, 76.71; H, 9.59; N, 6.39%.

¹ Manuscript received May 22, 1953.

Contribution from the Dominion Rubber Company Limited Research Laboratories, Guelph, Ont.

*All melting points are corrected.

Lycopodine

The solvent was removed from mother liquors resulting from the purification of alkaloid L35 and the residue extracted with several portions of boiling hexane. The somewhat concentrated extract, on being seeded with lycopodine, deposited this base in colorless crystals which melted at 116° either alone or in admixture with lycopodine.

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ULTRAVIOLET ABSORPTION SPECTRA OF ARYL SUBSTITUTED UREAS¹

By J. P. PICARD² AND A. F. MCKAY³

ABSTRACT

Absorption spectra of a number of substituted aryl- and *sym*-diarylureas have been determined in ethanol. As conjugation in the chromophores increased, a gradual displacement of the maxima of the conjugative absorption band towards the visible occurred. This displacement was accompanied by a progressive increase in intensity of absorption. The effect on the absorption spectra of replacing hydrogen of the aryl substituents by alkoxy, methyl, or halogeno groups is discussed. A relationship between the inductive effect of these groups and their influence on the absorption spectra is indicated.

INTRODUCTION

The ultraviolet absorption spectra of a small number of arylureas have been reported (4, 6, 14, 15) in the literature. Schroeder *et al.* (14) have measured the ultraviolet absorption spectra of 26 arylureas. They were interested in the use of these spectra for the identification of stabilizers as well as the identification of their transformation products formed during the aging of propellants. Their data on the two arylureas, *sym*-diphenylurea and 1-ethyl-3-phenylurea, which are reported also in this paper, are in good agreement with the present studies.

Grammaticakis (4, 6)¹ has reported the ultraviolet absorption spectra of a few arylureas in his investigation of the effect of ortho substituents on the absorption of N-alkyl, N-acyl, and N-carbamyl derivatives of arylamines and Stuckey (15) has reported the ultraviolet absorption spectrum for cinnamylurea. These investigations have been extended to include a large number of arylureas in an attempt to correlate their ultraviolet absorption spectra with structural changes.

GENERAL DISCUSSION OF ULTRAVIOLET ABSORPTION SPECTRA OF ARYLUREAS

The arylureas in ethanol exhibit two absorption maxima in the middle ultraviolet region (220–400 m μ). Maximum I of low intensity (benzenoid absorption) is closer to the visible end of the spectrum than maximum II (conjugative absorption) of high intensity. A third maximum would be expected below 220 m μ owing to ethylenic absorption but this region of the spectrum was not investigated in the present studies.

Benzene possesses absorption maxima of low intensities (7) (cf. Fig. 1) and



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the canonical structures I and II are considered contributing forms to this absorption. When one of the hydrogens of benzene is replaced by NH_2 to give aniline, conjugation of the free electron pair of the nitrogen with the benzene

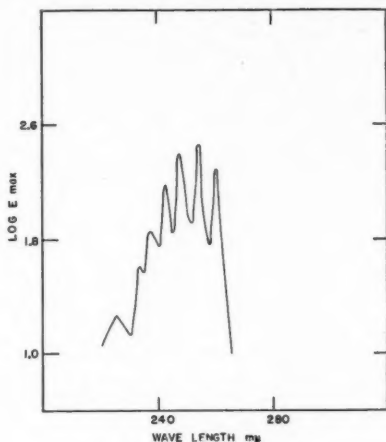
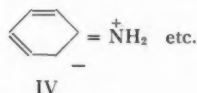
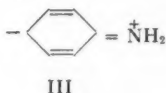
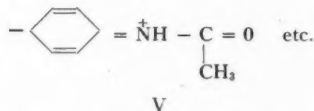


FIG. 1. Benzene.

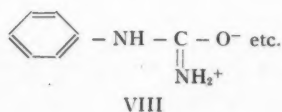
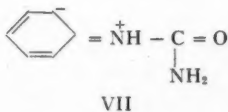
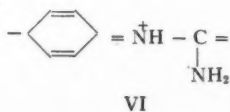
nucleus can occur. This conjugation causes an appearance of a new absorption maximum at $232 \text{ m}\mu$ ($E_{\text{max}} 8300$) along with an increase in intensity of absorption in the vicinity of the other maxima (benzenoid absorption). The latter absorption has a maximum at $280 \text{ m}\mu$ with a molar extinction coefficient of 1570 (8) (Curve A, Fig. 2). Contributing forms to this absorption are III and IV etc.



A further extension of the conjugative systems occurs in acetanilide (5) as shown in electronic structures V etc.



Acetanilide has absorption maxima at 277 (shoulder) and $240 \text{ m}\mu$ (Curve B, Fig. 2). Thus maximum II has increased in intensity and undergone a batho-



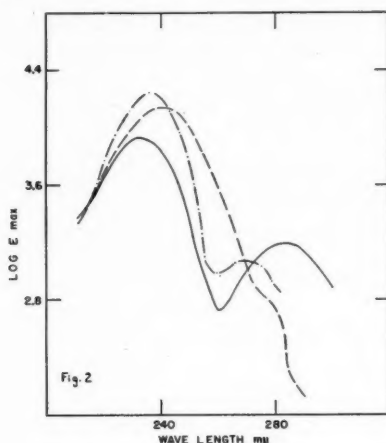


FIG. 2. Curve A — Aniline.
Curve B - - Acetanilide.
Curve C - · - Phenylurea.

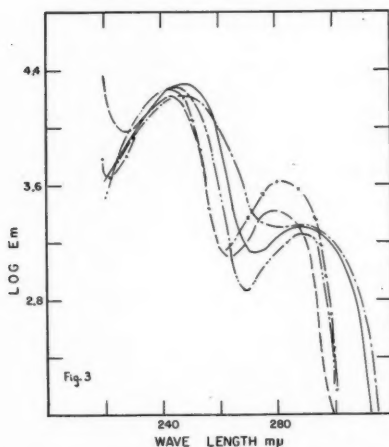


FIG. 3. Curve A — 1-*p*-Phenetyl-2-imidazolidone.
Curve B - - 2-*p*-Phenetyl-amino-2-oxazoline.
Curve C - · - 2-*p*-Phenetyl-3-ethylurea.
Curve D - - 1-*m*-Phenetyl-3-ethylurea.
Curve E - x - 1-*o*-Phenetyl-3-ethylurea.

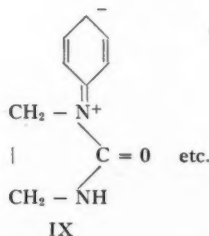
chromic shift of 8 $m\mu$. If the methyl group of acetanilide is replaced by an amino group to give an arylurea, a slight hypsochromic shift in the wave lengths of the absorption maxima (cf. phenylurea, Ref. 14 and Curve C, Fig. 2) occur. There is also a small increase in E_{\max} . It is apparent from the canonical forms VI, VII, VIII etc., which would be considered as participating in the absorption, that there is little or no extension of conjugation over that existent in acetanilide. It is considered that the effect of structure VIII and similar struc-

tures on absorption is unimportant relative to forms VI and VII. Table I shows that the monoarylureas have maxima at 240–249 m μ and 270–292 m μ . If cyclic ureas, e.g., ethyleneurea, are substituted on one of the nitrogens with an aryl group then the ultraviolet absorption maxima of these derivatives occur at

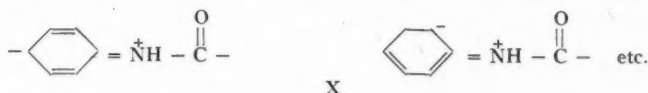
TABLE I
ABSORPTION SPECTRA OF ARYLUREAS
WAVE LENGTHS AND INTENSITIES OF THE MAXIMA

| Compound | λ_{\max} I, m μ | log E_{\max} I | λ_{\max} II, m μ | log E_{\max} II |
|---|--------------------------------|------------------|---------------------------------|-------------------|
| 1-Phenyl-3-ethylurea | 275 | 3.02 | 240 | 4.30 |
| 1- <i>p</i> -Tolyl-3-ethylurea | 281 | 3.11 | 243 | 4.37 |
| 1- <i>m</i> -Tolyl-3-ethylurea | 275 | 3.03 | 240 | 4.24 |
| 1- <i>o</i> -Tolyl-3-ethylurea | 270 | 2.90 | 240 | 4.08 |
| 1- <i>p</i> -Chlorophenyl-3-ethylurea | 284 | 3.12 | 248 | 4.40 |
| 1- <i>m</i> -Chlorophenyl-3-ethylurea | 282 | 3.09 | 246 | 4.25 |
| 1- <i>o</i> -Chlorophenyl-3-ethylurea | 280 | 3.12 | 242 | 4.30 |
| 1- <i>p</i> -Bromophenyl-3-ethylurea | | Inflection | 249 | 4.42 |
| 1- <i>p</i> -Anisyl-3-ethylurea | 292 | 3.23 | 244 | 4.25 |
| 1- <i>o</i> -Anisyl-3-ethylurea | 282 | 3.64 | 242 | 4.25 |
| 1- <i>p</i> -Phenetyl-3-ethylurea | 291 | 3.27 | 245 | 4.30 |
| 1- <i>m</i> -Phenetyl-3-ethylurea | 280 | 3.44 | 242 | 4.22 |
| 1- <i>o</i> -Phenetyl-3-ethylurea | 282 | 3.63 | 242 | 4.27 |
| 1- <i>p</i> -Tolyl-3- β -chloroethylurea | 280 | 2.98 | 243 | 4.26 |
| 1- <i>p</i> -Anisyl-3- β -chloroethylurea | 288 | 3.24 | 243–245 | 4.24 |
| 1- <i>p</i> -Phenetyl-3- β -chloroethylurea | 285 | 3.22 | 245 | 4.27 |
| 1- <i>p</i> -Tolylurea | 280 | 2.97 | 240 | 4.22 |
| 1- <i>p</i> -Anisylurea | 289 | 3.23 | 243 | 4.21 |
| 1- <i>p</i> -Phenetylurea | 289 | 3.21 | 241–243 | 4.23 |

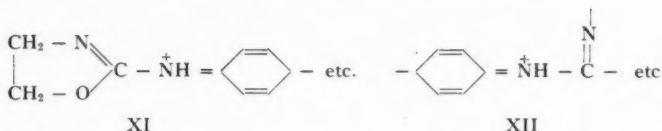
about the same wave lengths as the corresponding monoarylureas. This is to be expected because the electronic structures (IX) contributing to absorption in the cyclic aryl substituted areas possess the same conjugative



system (X) (chromophore) as the arylureas and as acetanilide. Furthermore



examination of the 2-arylamino-2-oxazolines (XI) discloses the participation of chromophores (XII) similar to XI in the absorption of these compounds.



The exchange of O in chromophore X for N in chromophore XII has little if any effect on the observed ultraviolet absorption spectra of these compounds. An examination of the data in Tables I and III and Curves A, B, and C of Fig. 3 indicate that the corresponding monoarylureas, 1-aryl-2-imidazolidones and 2-arylamino-2-oxazolines possess similar absorption characteristics as well as molar extinction coefficients of the same order.

Finally the symmetrical substitution of urea with two aryl groups gives new chromophores with extended conjugative systems.



This in accord with expectation causes bathochromic and hyperchromic shifts in maximum II. The effect on maximum I is discussed below in detail. Thus a gradual extension of the conjugative system from benzene through aniline to diarylureas effects a progressive bathochromic shift in maximum II and a progressive increase in its molar extinction coefficient. On the other hand the wave lengths of maximum I (benzenoid absorption) change with substitution on the benzene ring. The molar extinction coefficients of maximum I are much higher in the *sym*-diarylureas than the monoarylureas (cf. Tables I and IV).

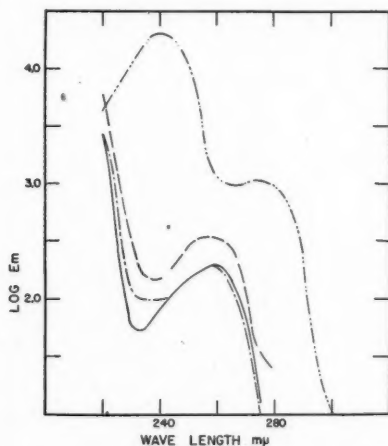


FIG. 4. Curve A — 1-β-Phenylethyl-3-ethylurea.
 Curve B - - - 1-Benzyl-3-ethylurea.
 Curve C . . . *sym*-Di-benzylurea.
 Curve D - · - · 1-Phenyl-3-ethylurea.

MONOARYLUREAS

The corresponding arylureas, 1-aryl-3-alkylureas and 1-benzyl-3-arylureas have similar maxima. Maximum II lies between 240 and 249 $m\mu$ while maximum I occurs between 270 and 292 $m\mu$. If a methylene group is placed between the phenyl and urea group as in 1-benzyl-3-ethylurea, the maximum at 240 $m\mu$ disappears leaving only the maximum at 260 $m\mu$ (cf. Fig. 4) owing to the benzenoid absorption. This absorption maximum occurs at the same wave length as the absorption maximum of toluene. Thus the conjugation between the phenyl and urea has been eliminated by insertion of the methylene group. The molar extinction coefficient of λ_{\max} of *sym*-dibenzylurea (382) is just about twice that of 1-benzyl-3-ethylurea.

The effect of substitution in the benzene ring on the absorption of arylureas is quite uniform. In general the wave lengths of maxima I and II for para and meta substituted arylureas increase in the following order



With ortho substitution the wave length of maximum I increases in the order



while the increase of wave length of maximum II is



Also the wave lengths of maxima I and II of substituted arylureas generally decrease in the order $p > m > o$. However the wave length of the λ_{\max} of the meta substituted compound may be the same as either the *p*- or *o*-substituted compound. This order does not hold for the intensities of absorption. When an alkoxy group is substituted for a hydrogen on the benzene ring, the intensities of absorption of maximum I decrease in the order $o > m > p$ while there is very little change in the intensities of maximum II (cf. Curves C, D, and E (Fig. 3)). This order of decrease of maximum I is just reversed in the case of tolylureas and halogenophenylureas, viz $p > m > o$ (cf. Curves A, B, and C (Fig. 5)). Also with the methyl and halogen substituted arylureas the intensities of maximum II in general decrease in the order $p > m > o$ (cf.

TABLE II
ABSORPTION SPECTRA OF 1-BENZYL-3-ARYLUREAS
WAVE LENGTHS AND INTENSITIES OF THE MAXIMA

| Compound | $\lambda_{\max I}$, $m\mu$ | $\log E_{\max I}$ | $\lambda_{\max II}$, $m\mu$ | $\log E_{\max II}$ |
|--|--------------------------------|-------------------|---------------------------------|--------------------|
| 1-Benzyl-3- <i>p</i> -tolylurea | 280 | 3.06 | 245 | 4.34 |
| 1-Benzyl-3- <i>m</i> -tolylurea | | Inflection | 245 | 4.29 |
| 1-Benzyl-3- <i>o</i> -tolylurea | | Inflection | 240 | 4.18 |
| 1-Benzyl-3- <i>p</i> -anisylurea | 290 | 3.22 | 245 | 4.30 |
| 1-Benzyl-3- <i>m</i> -anisylurea | 280 | 3.47 | 245 | 4.24 |
| 1-Benzyl-3- <i>p</i> -phenetylurea | 290 | 3.22 | 245 | 4.31 |
| 1-Benzyl-3- <i>p</i> -chlorophenylurea | 280 | 3.13 | 248 | 4.46 |
| 1-Benzyl-3- <i>p</i> -bromophenylurea | | Inflection | 250 | 4.42 |
| 1-Benzyl-3- <i>o</i> -bromophenylurea | 280 | 3.09 | 245 | 4.22 |

Tables I and II). These effects of substitution on maxima I and II also hold for the diarylureas.

If it is considered that substituents in the benzene ring of arylureas influence the ease of formation of electronic structures having the N conjugated with the benzene ring, there should be some consistency in behavior with respect to their electromeric or inductive effects. If the effect of the alkoxy groups is assumed to be due to an electromeric effect then the decrease in order of intensities of maximum I would be expected to follow the order $o > p > m$ or $o, p > m$. On the other hand an inductive effect would be expected to affect the order of decrease in intensities in such a manner that $o > m > p$ for

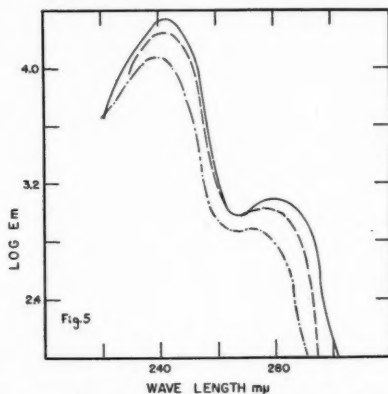


FIG. 5. Curve A — 1-*p*-Tolyl-3-ethylurea.
Curve B - - 1-*m*-Tolyl-3-ethylurea.
Curve C - · - 1-*o*-Tolyl-3-ethylurea.

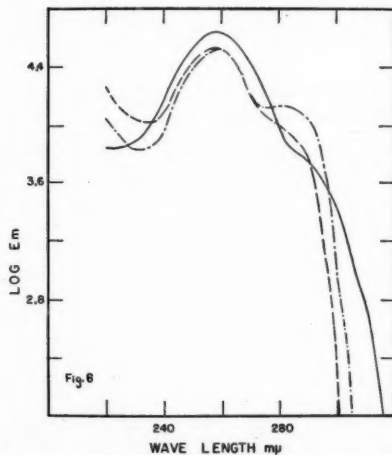


FIG. 6. Curve A — 1-*p*-Anisyl-3-*p*-tolylurea.
Curve B - - 1-*m*-Anisyl-3-*p*-tolylurea.
Curve C - · - 1-*o*-Anisyl-3-*p*-tolylurea.

alkoxy groups, while methyl groups would be expected to have the opposite effect on order, viz $p > m > o$. An examination of Figs. 3 and 5 and Tables I and II will indicate that substituents of arylureas affect the order of intensity variation in exactly the manner predicted on the basis of the inductive effect.⁴ Table IV and Figs. 4 and 5 also show that the effect of substituents in diphenylurea is the same as in monophenylureas. Fig. 6 shows that the curve for 1-*p*-anisyl-3-*p*-tolylurea possesses an inflection at the wave length where maximum I would be expected to appear. As the methoxy substituent is moved from the *p*- to the *m*-position, this inflection acquires a higher intensity of absorption and finally in the *o*-isomer two distinct maxima appear. The final absorption of this maximum has a higher intensity of absorption than the inflections of the other two curves. It can be seen also in Fig. 5 that the one maximum and inflection of the curve of di-*p*-anisylurea is resolved into two maxima in di-*m*-anisylurea and di-*o*-anisylurea. Moreover in agreement with the monoarylureas, the intensity of absorption of maximum I decreases in the order $o > m > p$.

The inclusion of the arylurea group in a ring structure as in 1-*p*-phenetyl-2-imidazolidone and 2-*p*-phenetyl-amino-2-oxazoline causes a slight displacement of the whole absorption curve towards the visible end of the spectrum (compare Curves A, B, and C of Fig. 3). However, cyclization has very little effect on the position of the maxima. There occurs a slight increase in the intensity of absorption but it is not pronounced. The absorption maxima of

TABLE III
ABSORPTION SPECTRA OF 1-ARYL-2-IMIDAZOLIDONES
WAVE LENGTHS AND INTENSITIES OF THE MAXIMA

| Compound | $\lambda_{\max I}$, m μ | $\log E_{\max I}$ | $\lambda_{\max II}$, m μ | $\log E_{\max II}$ |
|---------------------------------------|---------------------------------|-------------------|----------------------------------|--------------------|
| 1-Phenyl-2-imidazolidone | | Inflection | 245 | 4.28 |
| 1- <i>p</i> -Tolyl-2-imidazolidone | 280 | 3.11 | 247 | 4.29 |
| 1- <i>p</i> -Anisyl-2-imidazolidone | 290 | 3.42 | 247 | 4.32 |
| 1- <i>p</i> -Phenetyl-2-imidazolidone | 290 | 3.30 | 247 | 4.31 |

1-aryl-2-imidazolidones (Table III) should be compared with the absorption maxima of 1-aryl-3-ethylureas (Table I).

DIARYLUREAS

The majority of the diarylureas studied displayed only one absorption maximum. This has not been due to a disappearance of the band characteristic of benzenoid absorption but rather to a coalescence of this band with the conjugative absorption band. This has resulted in the formation of a rather broad and unsymmetrical absorption band (cf. Figs. 8 and 9). In other cases (cf. Curve A, Fig. 7) an inflection appears on the shoulder of maximum II, while in the case of *sym*-di-*m*-alkoxyphenylureas and *sym*-di-*o*-alkoxyphenyl-

⁴ This apparent relationship of the inductive effect to absorption intensities will be investigated further.

ureas the absorption bands are sufficiently separated to give two distinct maxima (cf. Curves *B* and *C* (Fig. 7)). When maximum I appears in the

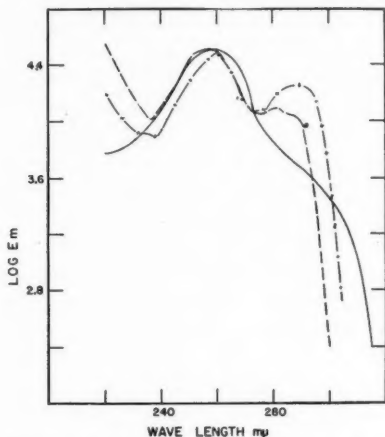


FIG. 7. Curve *A* — 1,3-Di-*p*-anisylurea.
Curve *B* - - 1,3-Di-*m*-anisylurea.
Curve *C* - x - 1,3-Di-*o*-anisylurea.

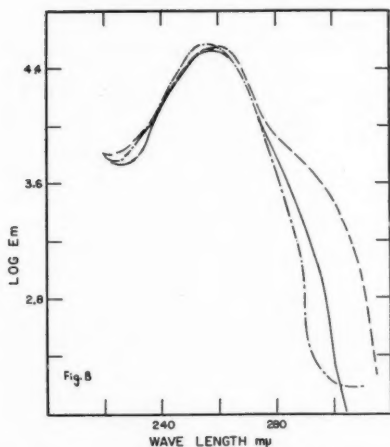


FIG. 8. Curve *A* — 1,3-Di-*p*-tolylurea.
Curve *B* - - 1,3-Di-*p*-phenethylurea.
Curve *C* - - - 1,3-Diphenylurea.

diarylureas it has a much larger molar extinction coefficient (ca. 12,000–15,000) than the corresponding maximum in monoarylureas (E_{\max} 1000–3000). Maximum I appears to be pushed up by the large conjugative absorption. This separation of maximum I and II in the *sym*-di-*m*- and di-*o*-alkoxyphenylureas is not due to steric hindrance. Similarly substituted ureas having the

alkoxy groups replaced by the larger halogeno group do not have this same degree of resolution of the two maxima (cf. Fig. 9 and Table IV). The inductive

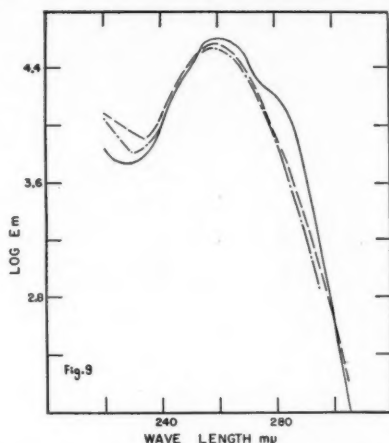


FIG. 9. Curve A — 1-*p*-Chlorophenyl-3-*p*-tolylurea.
Curve B - - 1-*m*-Chlorophenyl-3-*p*-tolylurea.
Curve C - x - 1-*o*-Chlorophenyl-3-*p*-tolylurea.

effect of substituents in relation to their influence on maximum I was discussed above.

It is not easy to summarize the effects of *unsym*-substitution in *sym*-diphenylurea. However, the data in Table IV indicate that there is a definite adherence to the above discussed generalities.

The molar extinction coefficients of the monoaryurea including the 1-aryl-2-imidazolidones and 2-arylamino-2-oxazolines vary in general from 16,500–25,000. These values are approximately doubled in the correspondingly substituted *sym*-diarylureas.

It will be noted from curves of Figs. 3 and 7 that maxima I and II are sometimes broad and unsymmetrical. These maxima are quite likely the result of coalescence of two or more bands. An attempt will be made to further resolve these absorption bands by measuring the absorption spectra of some of these aryureas at lower temperatures.

EXPERIMENTAL⁵

Arylureas

The aryureas used in the ultraviolet absorption studies were analytically pure samples. The method of preparation of the majority of these compounds and their melting points have been published (11). The other known aryureas were prepared in the same manner.

1-Aryl-3- β -chloroethylureas

A benzene solution of β -chloroethylamine was prepared as previously (9)

⁵ All melting points are uncorrected. Microanalyses by Mr. C. W. Beazley, Skokie, Ill.

TABLE IV
ABSORPTION SPECTRA OF 1,3-DIARYLUREAS
WAVE LENGTHS AND INTENSITIES OF THE MAXIMA

| Compound | $\lambda_{\max I}$, m μ | log $E_{\max I}$ | $\lambda_{\max II}$, m μ | log $E_{\max II}$ |
|---|---------------------------------|------------------|----------------------------------|-------------------|
| 1,3-Diphenylurea | | | 255 | 4.57 |
| 1,3-Di- <i>p</i> -tolylurea | | | 257 | 4.52 |
| 1- <i>m</i> -Tolyl-3- <i>p</i> -tolylurea | | | 258 | 4.52 |
| 1- <i>o</i> -Tolyl-3- <i>p</i> -tolylurea | | | 255 | 4.47 |
| 1,3-Di- <i>m</i> -tolylurea | | | 258 | 4.72 |
| 1,3-Di- <i>o</i> -tolylurea | | | 252 | 4.32 |
| 1- <i>p</i> -Anisyl-3- <i>p</i> -tolylurea | | Inflection* | 258 | 4.63 |
| 1- <i>m</i> -Anisyl-3- <i>p</i> -tolylurea | | Inflection | 258 | 4.53 |
| 1- <i>o</i> -Anisyl-3- <i>p</i> -tolylurea | 282 | 4.15 | 260 | 4.52 |
| 1- <i>p</i> -Phenetyl-3- <i>p</i> -tolylurea | | | 259 | 4.55 |
| 1- <i>m</i> -Phenetyl-3- <i>p</i> -tolylurea | | Inflection | 259 | 4.54 |
| 1- <i>o</i> -Phenetyl-3- <i>p</i> -tolylurea | 282 | 4.13 | 260 | 4.52 |
| 1- <i>p</i> -Chlorophenyl-3- <i>p</i> -tolylurea | | Inflection | 262 | 4.61 |
| 1- <i>m</i> -Chlorophenyl-3- <i>p</i> -tolylurea | | | 260 | 4.57 |
| 1- <i>o</i> -Chlorophenyl-3- <i>p</i> -tolylurea | | | 258 | 4.54 |
| 1- <i>p</i> -Bromophenyl-3- <i>p</i> -tolylurea | | | 263 | 4.61 |
| 1- <i>m</i> -Bromophenyl-3- <i>p</i> -tolylurea | | | 260 | 4.57 |
| 1- <i>o</i> -Bromophenyl-3- <i>p</i> -tolylurea | | | 260 | 4.51 |
| 1- <i>m</i> -Tolyl-3- <i>p</i> -anisylurea | | | 258-260 | 4.49 |
| 1- <i>o</i> -Tolyl-3- <i>p</i> -anisylurea | | | 255 | 4.41 |
| 1,3-Di- <i>p</i> -anisylurea | | Inflection | 258-260 | 4.51 |
| 1- <i>m</i> -Anisyl-3- <i>p</i> -anisylurea | | Inflection | 258 | 4.49 |
| 1- <i>o</i> -Anisyl-3- <i>p</i> -anisylurea | 283 | 4.18 | 260 | 4.52 |
| 1- <i>p</i> -Phenetyl-3- <i>p</i> -anisylurea | | Inflection | 260 | 4.54 |
| 1- <i>m</i> -Phenetyl-3- <i>p</i> -anisylurea | | Inflection | 258 | 4.49 |
| 1- <i>o</i> -Phenetyl-3- <i>p</i> -anisylurea | 283 | 4.09 | 258-260 | 4.43 |
| 1- <i>p</i> -Chlorophenyl-3- <i>p</i> -anisylurea | | | 263 | 4.56 |
| 1- <i>m</i> -Chlorophenyl-3- <i>p</i> -anisylurea | | | 260 | 4.51 |
| 1- <i>o</i> -Chlorophenyl-3- <i>p</i> -anisylurea | | | 258-260 | 4.47 |
| 1- <i>p</i> -Bromophenyl-3- <i>p</i> -anisylurea | | | 262-264 | 4.59 |
| 1- <i>m</i> -Bromophenyl-3- <i>p</i> -anisylurea | | | 260 | 4.50 |
| 1- <i>o</i> -Bromophenyl-3- <i>p</i> -anisylurea | | | 258-260 | 4.44 |
| 1,3-Di- <i>m</i> -anisylurea | 282 | 4.10 | 257 | 4.51 |
| 1,3-Di- <i>o</i> -anisylurea | 288 | 4.25 | 260 | 4.49 |
| 1- <i>m</i> -Tolyl-3- <i>p</i> -phenetylurea | | | 260 | 4.53 |
| 1- <i>o</i> -Tolyl-3- <i>p</i> -phenetylurea | | | 255 | 4.46 |
| 1- <i>m</i> -Anisyl-3- <i>p</i> -phenetylurea | 283 | 4.19 | 260 | 4.51 |
| 1- <i>o</i> -Anisyl-3- <i>p</i> -phenetylurea | 282 | 4.18 | 260 | 4.52 |
| 1,3-Di- <i>p</i> -phenetylurea | | Inflection | 260 | 4.54 |
| 1- <i>m</i> -Phenetyl-3- <i>p</i> -phenetylurea | | Inflection | 260 | 4.55 |
| 1- <i>o</i> -Phenetyl-3- <i>p</i> -phenetylurea | 283 | 4.15 | 260 | 4.49 |
| 1- <i>p</i> -Chlorophenyl-3- <i>p</i> -phenetylurea | | | 262 | 4.62 |
| 1- <i>m</i> -Chlorophenyl-3- <i>p</i> -phenetylurea | | | 260 | 4.56 |
| 1- <i>o</i> -Chlorophenyl-3- <i>p</i> -phenetylurea | | | 258-260 | 4.45 |
| 1- <i>p</i> -Bromophenyl-3- <i>p</i> -phenetylurea | | | 263-265 | 4.58 |
| 1- <i>m</i> -Bromophenyl-3- <i>p</i> -phenetylurea | | | 260-263 | 4.53 |
| 1- <i>o</i> -Bromophenyl-3- <i>p</i> -phenetylurea | | | 258-260 | 4.46 |
| 1,3-Di- <i>m</i> -phenetylurea | 282 | 4.11 | 257 | 4.52 |
| 1- <i>p</i> -Tolyl-3-phenylurea | | | 258-260 | 4.56 |
| 1- <i>p</i> -Anisyl-3-phenylurea | | | 258-260 | 4.53 |
| 1- <i>p</i> -Phenetyl-3-phenylurea | | | 258 | 4.51 |
| 1- <i>p</i> -Chlorophenyl-3-phenylurea | | | 260 | 4.55 |

* These inflections appear in the wave length region of maximum I but no attempt has been made to assign wave lengths to them.

described. To this solution 0.0647 mole of an arylisocyanate was added. Almost immediately white precipitates of the products were obtained in good yields (95-98%). Purification was effected by one crystallization from 95%

ethanol. In this way the following 1-aryl-3 β -chloroethylureas were prepared. *1-p-Tolyl-3 β -chloroethylurea* (m.p. 178–179° C.). Calc. for $C_{10}H_{13}ClN_2O$: C, 56.60; H, 6.13; Cl, 16.70%. Found: C, 56.46; H, 6.27; Cl 17.02%. *1-p-Anisyl-3 β -chloroethylurea* (m.p. 160–160.3° C.). Calc. for $C_{10}H_{13}ClN_2O_2$: C, 52.60; H, 5.69; Cl, 15.54%. Found: C, 52.75; H, 5.71; Cl, 15.55%. *1-p-Phenetyl-3 β -chloroethylurea* (m.p. 149–151° C.). Calc. for $C_{11}H_{15}ClN_2O_2$: C, 54.43; H, 6.19; Cl, 14.64%. Found: C, 54.65; H, 6.32; Cl, 14.65%.

1-Aryl-2-imidazolidones

The preparation of 1-phenyl-2-imidazolidone (2, 10) and 1-*p*-anisyl-2-imidazolidone (12) by the respective cyclizations in alkaline solutions of 1-phenyl-3 β -chloroethylurea and 1-*p*-anisyl-3 β -chloroethylurea have been described. In a similar manner 1-*p*-tolyl-2-imidazolidone (13) (m.p. 196.5–197° C.) and 1-*p*-phenetyl-2-imidazolidone (13) (m.p. 211.5–212° C.) were prepared in yields of 85.9 and 86.5% respectively.

2-Arylamino-2-oxazolines

2-*p*-Phenetyl-amino-2-oxazoline (m.p. 152.5–153° C.) was prepared from 1-*p*-phenetyl-3 β -bromoethylurea (m.p. 132° C.) in 72% yield by the method of Englemann (1). Englemann reports a melting point of 151° C. while Gebauer (3) gives a melting point of 153° C. Calc. for $C_{11}H_{14}N_2O_2$: N, 13.59%. Found: N, 13.70%.

2-*p*-Tolyl-amino-2-oxazoline (m.p. 165.2–166° C.) was prepared similarly from 1-*p*-tolyl-3 β -bromoethylurea (160–161° C.) in 62.6% yield. Calc. for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.82; N, 15.91%. Found: C, 68.32; H, 6.82; N, 16.18%.

DETERMINATION OF SPECTRA

The ultraviolet absorption spectra were measured in 95% ethanol with a Beckman Quartz Spectrophotometer, Model DU.

The concentrations of the solutions ranged from 2×10^{-4} to 3.00×10^{-5} mole/liter. In the majority of cases only one determination was made for each urea. However, several determinations at different concentrations were performed on about eight of the urea derivatives and the reproducibility of spectral measurements ascertained. Thus slight variations in absorption maxima and molecular extinction coefficients (E_m) are neglected in the above discussion. E_{max} refers to the molecular extinction coefficient at the wave length of maximum absorption.

ACKNOWLEDGMENTS*

The authors wish to thank Dr. C. Sandorfy of the National Research Council, Canada, for measuring the spectrum of 1,3-di-*o*-anisylurea and Messrs. H. E. Rooney and A. M. Bedard of Canadian Armament Research and Development Establishment for measuring the spectra of the ureas. We also thank Mr. W. G. Hatton of Defence Research Chemical Laboratories for his assistance in the preparation of a number of the urea derivatives.

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THE USE OF ISOTOPE DILUTION IN DETERMINATION OF GEOLOGIC AGE OF MINERALS¹

BY R. H. TOMLINSON AND A. K. DAS GUPTA²

ABSTRACT

The mass spectrometer has been used for the estimation of trace quantities of rubidium and strontium. The isotope dilution technique developed by Aldrich has been extended so that 0.01% of rubidium and 0.0001% strontium have been analyzed with 100 mgm. of mineral. The use of small quantities for mass spectrometric determination allows the use of easily available fission strontium and rubidium. The radioactivity of the fission strontium also simplifies the chemical manipulation. No chemical separation from the mineral was required for the rubidium but the strontium was concentrated by ion exchange methods. Ages are presented for one lepidolite and two biotite minerals and their ages compared to those found by other methods. With one of the biotites the effect of weathering on the fractionation of rubidium from strontium has been studied.

INTRODUCTION

The possibility of measuring age of minerals by using the decay of naturally occurring rubidium has been under investigation since 1937. Naturally occurring rubidium consists of the isotopes 85 and 87, of which Rb^{87} is radioactive and forms Sr^{87} by beta decay. Since the half life of Rb^{87} is of the order of 10^{10} years, which is very long compared to the age of the minerals under investigation, the age can be obtained from the following expression:

$$T(\text{age}) = \frac{\% \text{Sr}^{87} (\text{radiogenic})}{\% \text{Rb}^{87}} \cdot \frac{1}{\text{Decay const. of Rb}^{87}} \quad [1]$$

The accuracy of the determination of age will depend on the accuracy of determining the three factors involved: (i) % of radiogenic Sr^{87} , (ii) % of rubidium in the mineral, and (iii) the decay constant of Rb^{87} . It is imperative that weathering has not washed out either rubidium or radiogenic Sr^{87} .

Rubidium though present in traces in many minerals does not form any minerals of its own. The highest content of rubidium is found in the lepidolites in which the Rb_2O content varies from 0.3 to 3.0%. The accurate determination of rubidium content by purely chemical methods, particularly in samples where the percentage may be only of the order of 10^{-2} , is bound to be unreliable. Spectrographic methods have been found more suitable (1).

The determination of Sr^{87} has presented great difficulties. Even in the older minerals the content of radiogenic Sr^{87} would be about 1/100 that of Rb^{87} which itself is 27.2% of the total rubidium. In minerals where the percentage of rubidium is only in the region of 0.01%, as in many of the biotites, the percentage of radiogenic Sr^{87} would be expected to be about 0.0001 at best and is liable to be mixed with normal strontium. Under these conditions, accurate determination of radiogenic Sr^{87} has not been reported.

This paper presents a method of estimating both Rb^{87} and Sr^{87} (radiogenic) even when they are present in very small quantities mixed with normal

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strontium, by using the technique of isotopic dilution along with the mass spectrometer (6). The mass spectrometer gives the ratio of the isotopes of an element, but it does not give any direct information as to the actual amount of a particular isotope. By addition to the sample to be analyzed of a known quantity of a single isotope of the element, the mass spectrometric ratio of the resultant mixture of isotopes can then be utilized to obtain the amount of each isotope. Since the isotopic ratios remain essentially constant through all chemical procedures, losses during manipulation do not affect the result. Whereas it is simplest to use a single separated isotope, any isotopic mixture whose isotopic abundance is different from that in nature may be used.

Aldrich *et al.* (2, 4) have reported a method for determination of the ages by the strontium method using the isotope dilution technique. Working only with lepidolites, in which the rubidium content is high, analyses were accomplished with 3-gm. samples. In this work 100-mgm. samples were found adequate even when the rubidium content was of the order of 10⁻²⁰%. This makes possible age determination of minerals hitherto beyond reach of any of the methods in use.

EXPERIMENTAL

Mass Spectrometry

The mass spectrometer used was a conventional 90° sector instrument with magnetic scanning and a hot filament ion source (5). For strontium analysis it was found that a platinum plated tungsten filament was most efficient. Suitable mass spectrograms were obtained with 0.5 µgm. of strontium and 0.01 µgm. of rubidium, although considerably smaller quantities could be used.

Preparation and Standardization of Sr⁹⁰ and Fission Rb Solutions

Radioactive Sr⁹⁰ obtained from the commercial products division of Atomic Energy of Canada Limited was diluted so that 100 ml. of the solution contained about two millicuries of activity. The ratio of Sr⁹⁰/Sr⁸⁸ was measured both for this solution, and for a mixture of 10 ml. of the same solution with 0.673 µgm. of natural strontium added. The results are shown in Table I

TABLE I
STANDARDIZATION OF Sr⁹⁰ AND OF FISSION RB SOLUTIONS

| Sr ⁹⁰ solution | | Fission Rb solution | |
|--|------------------------------------|--|------------------------------------|
| Sample | Sr ⁹⁰ /Sr ⁸⁸ | Sample | Rb ⁸⁶ /Rb ⁸⁷ |
| Fission strontium | 1.255 ± .008 | Fission rubidium | 0.423 ± .003 |
| 10 ml. fission strontium + normal strontium contain- ing 0.556 µgm. Sr ⁸⁸ | 0.817 ± .007 | Natural rubidium | 2.68 ± .01 |
| | | 1 ml. fission Rb and 0.0142 µgm. natural Rb | 0.963 ± .003 |

from which it can be calculated that 5 ml. of fission strontium solution contained 0.650 µgm. Sr⁹⁰.

Fission rubidium, which is rich in Rb^{87} , was separated from the divalent and trivalent fission product ions by preferential elution from Dowex 50 ion exchange column using 0.3 *N* hydrochloric acid. The concentration of a stock solution of this was determined by a method similar to that used for Sr^{90} . From the data shown in Table I the concentrations of Rb^{87} and Rb^{85} in the stock solution are found to be 0.0123 $\mu\text{gm./ml.}$ and 0.00520 $\mu\text{gm. per ml.}$ respectively.

Separation and Estimation of Strontium

The weight of the sample required for an age determination will depend on the Rb content and on the age of the mineral. Ten milligrams of the lepidolite and 100 mgm. of the biotites were used for analysis. The minerals after repeated hydrofluoric acid treatment were taken into solution with hydrochloric acid and diluted to 50 ml. Separations of strontium were carried out on a 8 cm. column of Dowex-50 ion exchange resin in the NH_4^+ form. The general principles of ion exchange separation of inorganic cations are very well known, and have been summarized by Schubert (9). The solutions of the minerals are relatively rich in cations such as Fe^{+++} , Al^{+++} , K^+ , and Na^+ . The aim of the separations was to obtain strontium sufficiently free from these elements to give strontium spectrograms with the mass spectrometer. Five milliliters of the Sr^{90} solution was added to aliquots of every sample. Since it is desirable to have approximately the same amounts of Sr^{90} and radiogenic Sr^{87} in the mixture, the aliquot of the sample solution may have to be determined by a trial experiment. The mixture, after evaporation, is taken up in 5 ml. of 5% citric acid solution and transferred to the column. Two hundred milliliters of 5% citric acid adjusted to pH 3.6 with ammonium hydroxide was used to elute out all the trivalent ions along with Y^{90} , the radioactive daughter isotope of Sr^{90} . It was observed, by adding radioactive cesium, that the NH_4^+ concentration in the citric acid elutant was sufficient to move the monovalent ions. As an added precaution, however, 100 ml. of 0.6 *N* hydrochloric acid was run through the column to remove the last traces of the monovalent ions and to wash out the citric acid. Separating out the calcium, though possible at this stage, was not found necessary as the strontium obtained by eluting with 6 *N* hydrochloric acid was quite suitable for mass spectrometry.

To obtain the quantity of radiogenic Sr^{87} it is only necessary to determine the ratio radiogenic $\text{Sr}^{87}/\text{Sr}^{90}$. The mass 87 peak on the spectrogram may in addition to radiogenic Sr^{87} consist of a contribution from normal strontium together with any rubidium contamination. It was found possible to burn off rubidium at a somewhat lower temperature than is necessary to emit strontium ions. For this procedure to be effective it was required that all the sample to be analyzed be placed near the center of the filament. Even if the rubidium was not completely removed, a correction for the rubidium contamination could have been applied since the ratio of $\text{Rb}^{85}/\text{Rb}^{87}$ is known and since all the peak at mass 85 on the spectrogram is due to Rb^{85} . The presence of mass 86 is indicative of normal strontium in the sample. The

TABLE II
SUMMARY OF DATA FOR AGE DETERMINATIONS OF MINERALS

| Sample No. | Mineral | Geologic location | Pretreatment | Weight of treated sample, gm. | % Radiogenic Sr^{87} | % Rb^{87} | Age in 10^9 years |
|------------|---|--------------------------------|----------------------------|-------------------------------|-------------------------------|-------------------------------|---------------------|
| 1 | Leptidolite | Bob Ingersol Mine, S. Dakota | Washed with hot aqua regia | 0.00971 | $7.35 \pm .59 \times 10^{-3}$ | 4.49×10^{-1} | 1.39 |
| 2 | Biotite magnetically separated from uraninite | Sickle Lake, N.E. Saskatchewan | Unwashed | 0.0709 | $6.95 \pm .12 \times 10^{-4}$ | $1.80 \pm .01 \times 10^{-2}$ | 3.23 |
| 3 | Uraninite containing biotite | " | Washed with hot aqua regia | 0.9595 | $2.13 \pm .10 \times 10^{-4}$ | $5.00 \pm .04 \times 10^{-3}$ | 3.56 |
| 4 | Biotite magnetically separated from uraninite | " | Washed with cold HCl | 0.0196 | $8.90 \pm .42 \times 10^{-4}$ | $2.22 \pm .03 \times 10^{-3}$ | 3.36 |
| 5 | Biotite | Mt. Monadnock New Hampshire | Unwashed | 0.1068 | $1.81 \pm .20 \times 10^{-4}$ | $2.64 \pm .03 \times 10^{-2}$ | 0.57 |

ratio $\text{Sr}^{86}/\text{Sr}^{87}$ in normal strontium being known, the contribution of normal strontium to mass 87 is easily corrected for.

Determination of Rubidium

The phenomenon of "saturation of ion source" mentioned by Aldrich (3) was not observed. Even a sample containing 15% potassium, 4.6% sodium, and $1.84 \times 10^{-2}\%$ rubidium gave the ratio $2.68 \pm .01$ for $\text{Rb}^{85}/\text{Rb}^{87}$. Nier (7) has reported the ratio $2.68 \pm .02$ for the rubidium isotopes. Therefore it was considered unnecessary to isolate the rubidium for mass spectrometry. An aliquot of the mineral solution was diluted so as to give a rubidium concentration of about $0.01 \mu\text{gm. per ml.}$ The $\text{Rb}^{85}/\text{Rb}^{87}$ ratio obtained from a mixture of 1 ml. of this solution with 1 ml. of the standardized fission rubidium solution was used to calculate the percentage of rubidium in the sample.

RESULTS AND DISCUSSION

The percentages of Rb^{87} and Sr^{87} in the minerals analyzed, together with their ages calculated from equation [1] are presented in Table II. The value of the decay constant used was 1.195×10^{-11} as suggested by Ahrens (1), although slightly different values have been reported since. Ahrens by spectrometric determination of Sr/Rb ratios has reported 0.9 to 1.5 billion years as the ages of lepidolites obtained from the same area as sample 1 in Table II. The age of the uraninite has been found by the lead isotope method to be 1.9×10^9 years (Department of Geophysics, University of Toronto). The age obtained for the biotite separated from the uraninite being much older (Sample 2, Table II), it was necessary to find the effect of weathering. Two age determinations were carried out, one on a sample of the uraninite washed with boiling aqua regia, and the other on the separated biotite washed with cold 12 *N* hydrochloric acid. The ages (Samples 3 and 4, Table II) were not found to have altered appreciably even with these treatments which were considerably more drastic than is likely to have occurred in nature. The percentages of strontium and rubidium for the Samples 2, 3, and 4 cannot be directly compared since Sample 3 contained a large quantity of silica while Sample 4 was merely depleted of iron and other soluble constituents. The age of the biotite obtained from Mt. Monadnock (Sample 5, Table II) is also found to be high when compared to the age limits 0.25 to 0.40 billion years given for ores from this area by the lead isotope method (8).

It is noted that although the age determined for the lepidolite is in general agreement with that obtained from the spectrographic Sr/Rb ratio, the other ages are considerably greater than those obtained from the lead isotope method. Since it has been shown that weathering did not appreciably affect the strontium method, it can be concluded that apart from possible error in the Rb^{87} half life, the ages found are essentially correct.

For accurate analyses by the isotope dilution method, it is desirable to have about equal amounts of isotopic spike and the isotope to be estimated. Aldrich (2) for each age determination has used 50 $\mu\text{gm.}$ of strontium containing 65% Sr^{84} and 180 $\mu\text{gm.}$ of rubidium containing 89% Rb^{87} . These

quantities of isotopes are sufficient for 100 strontium and 10^4 rubidium analyses by the method described in this work. The use of small quantities has greatly simplified chemical separation of strontium and has made separation unnecessary for rubidium. A further advantage of using less than microgram quantities of spiking isotope is the possibility of using Sr^{90} , which because of its radioactivity, would necessitate special precautions if it were required in much greater quantities. Sr^{90} is a readily available, inexpensive fission product, which, being entirely absent in nature, makes the interpretation of the mass spectrograms simpler than those obtained with the use of enriched isotopic mixtures. Furthermore, in less than microgram quantities, the Sr^{90} , together with its daughter isotope Y^{90} , acts as a convenient tracer which greatly facilitates the handling of the sample.

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A NEW MECHANISM FOR PERSULPHATE OXIDATIONS¹

BY LEONARD S. LEVITT²

ABSTRACT

A new mechanism for oxidations by persulphate is presented, wherein it is postulated that the persulphate ion dissociates reversibly, by means of a heterolytic cleavage, into a sulphate ion and a molecule of sulphur tetroxide. Sulphur tetroxide is considered to be the active oxidizing species, combining reversibly with the substrate to form a complex whose subsequent decomposition gives the principal reaction products. The very small equilibrium concentration of sulphur tetroxide becomes the limiting factor in the rate of oxidation when a readily oxidizable substrate is present in relatively high concentration. The mechanism is applied to the data of Eager and Winkler for the oxidation of mercaptans, in which a limiting rate was attained above a certain mercaptan concentration. An empirical equation relating the rate constant to the mercaptan concentration is developed to fit the experimental data. Rate equations showing the rate dependence on mercaptan concentration are derived from the proposed mechanism and are found to be of the same form as the empirical equation. The mechanism is applied also to the persulphate oxidation of water.

INTRODUCTION

In the paper by Eager and Winkler entitled "The oxidation of mercaptans by potassium persulphate in homogeneous solution" (3), it was shown that a maximum or limiting rate was attained at a certain low mercaptan concentration, above which no further increase in mercaptan concentration resulted in an increased rate. The reaction was always first order, however, with respect to the measured persulphate concentration. A mechanism was proposed in which it was assumed that the first and rate-controlling step was the reversible dissociation, $S_2O_8^{2-} \rightleftharpoons 2 SO_4^{\cdot -}$. No rate equations showing the rate dependence on mercaptan concentration were derived, however.

Quite similar results have also been observed in the persulphate oxidation of organic sulphides (7) and sulfoxides (9), in both cases a limiting rate being attained.

In the present article is proposed a new mechanism for persulphate oxidations, the application of which leads to the development of rate equations of the required form, showing the rate dependence on the concentration of the sulphur compound oxidized. The new mechanism will be applied to the data of Eager and Winkler.

AN EMPIRICAL RATE EQUATION

Since a limiting value of the rate constant is attained at higher mercaptan concentrations, an equation of the following form is applicable:

$$-dP/dt = kP = [aS/(b + S)]P \quad [1]$$

where a and b are empirical constants, S is the mercaptan concentration,

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P is the persulphate concentration, and k is the observed rate constant. From Eq. 1, k is seen to be given by

$$k = aS/(b + S). \quad [2]$$

It is obvious from Eq. 2 that at very low mercaptan concentrations $S \ll b$ and

$$k = (a/b)S \quad [3]$$

the rate being proportional to the mercaptan concentration. On the other hand, at high mercaptan concentrations $S \gg b$, and

$$k = a. \quad [4]$$

In this case, then, the rate is independent of the mercaptan concentration.

The constants a and b may be evaluated from the experimental data in a number of ways. From Eq. 4, a is evidently equal to the experimentally

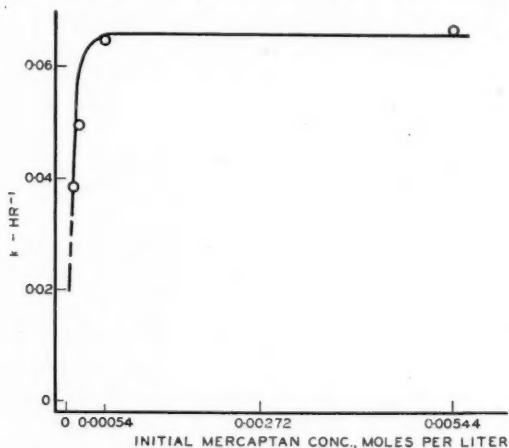


FIG. 1. Variation of k with n -dodecyl mercaptan concentration. Initial potassium persulphate concentration, 0.00153 mole per liter; temperature, $25.00 \pm 0.01^\circ\text{C}$.

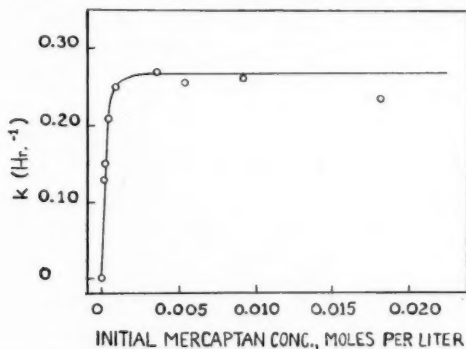


FIG. 2. Variation of k with n -dodecyl mercaptan concentration. Initial potassium persulphate concentration, 0.00153 mole per liter; temperature, $35.00 \pm 0.01^\circ\text{C}$.

determined maximum rate constant. The ratio a/b is seen from Eq. 3 to be the slope of the initial straight line portion of the plot of k vs. S (Figs. 1 and 2). In addition, it may be noted from Eq. 1 that b is equal to the mercaptan concentration at which the velocity of the reaction has attained one-half its limiting value.

An alternate and more accurate method of evaluating the empirical constants is as follows. Equation 2 may be rearranged to give

$$S/k = (b/a) + (S/a). \quad [5]$$

Thus, a plot of S/k vs. S should be a straight line with slope $1/a$ and intercept b/a . That a straight line does, indeed, result is evident from Figs. 3 and 4

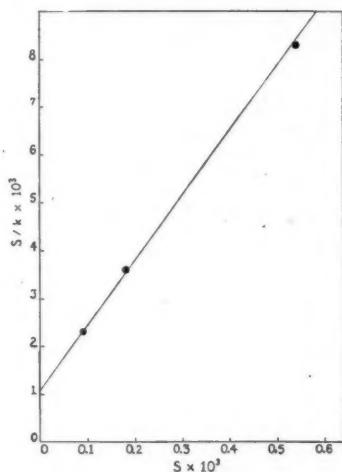


FIG. 3. Test of Equation 5 (at 25°).

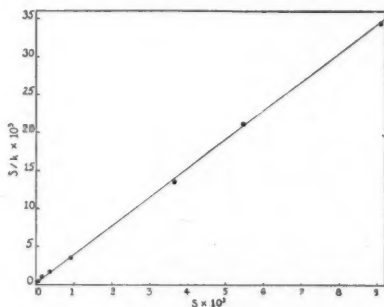


FIG. 4. Test of Equation 5 (at 35°).

in which such a plot has been made using the data for *n*-dodecyl mercaptan at 25°C. and at 35°C.

At 25°, the slope is equal to 14.3 and hence $a = 0.070$; the intercept is equal to 1.04×10^{-3} and thus $b = 7.3 \times 10^{-5}$. At 35°, the slope is 3.76 and the intercept 0.38, whence $a = 0.27$, and $b = 1.0 \times 10^{-4}$.

Substituting the numerical values for the constants a and b in Eq. 2, we have, at 25°

$$k = 0.070 S / (0.000073 + S) \quad [6]$$

and at 35°

$$k = 0.27 S / (0.00010 + S). \quad [6a]$$

The observed rate constants can thus be calculated from Equations 6 and 6a. Tables I and II give a comparison of the observed values of k at different mercaptan concentrations with the values calculated from Equations 6 and 6a. The agreement is seen to be satisfactory.

TABLE I
OBSERVED RATE CONSTANTS FOR THE OXIDATION OF *n*-DODECYL
MERCAPTAN AT 25°, AND THOSE CALCULATED USING EQ. 6.

| Mercaptan conc. (<i>M</i>) | <i>k</i> (hr. ⁻¹) | |
|---------------------------------|-------------------------------|-------|
| | Obs. | Calc. |
| 0.00009 | 0.0388 | 0.039 |
| 0.00018 | 0.0494 | 0.050 |
| 0.00054 | 0.0649 | 0.062 |
| 0.00544 | 0.0668 | 0.069 |

TABLE II
OBSERVED RATE CONSTANTS FOR THE OXIDATION OF *n*-DODECYL
MERCAPTAN AT 35°, AND THOSE CALCULATED USING EQ. 6a.

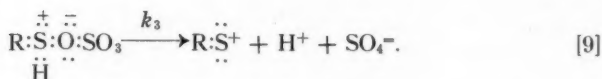
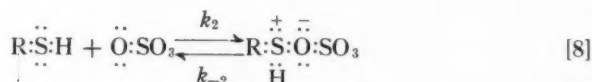
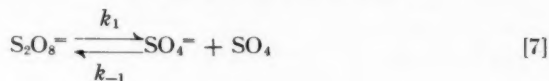
| Mercaptan conc. (<i>M</i>) | <i>k</i> (hr. ⁻¹) | |
|---------------------------------|-------------------------------|-------|
| | Obs. | Calc. |
| 0.00004 | 0.131 | 0.08 |
| 0.00018 | 0.154 | 0.17 |
| 0.00036 | 0.208 | 0.21 |
| 0.00091 | 0.246 | 0.24 |
| 0.00363 | 0.267 | 0.26 |
| 0.00544 | 0.255 | 0.26 |
| 0.00907 | 0.262 | 0.27 |
| 0.01815 | 0.233 | 0.27 |

THE NEW MECHANISM

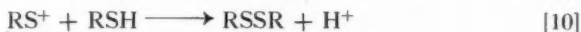
The nature of the rate dependence upon mercaptan concentration suggests a mechanism involving one or more reversible steps, one of which is rate-determining. The mechanism should account also for the retarding effect of sulphate ion on the rate.*

*Although its effect in the acetic acid solvent used by Eager and Winkler is not clear, the retardation of the rate brought about by sulphate in aqueous solution is well known (6).

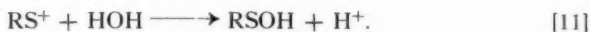
A mechanism in agreement with these requirements is as follows:



Only the final step is considered to be irreversible. Sulphate ion, if present initially, would retard the first step. The complex formed in Equation 8 may undergo the two reactions indicated. The ion RS^+ is here postulated to be the primary oxidation product of the mercaptan, and it might, in addition to being further oxidized, undergo such reactions as:



and



These reactions could be followed by further oxidation of the disulphide and of RSOH , which is not stable.

The molecule SO_4 , sulphur tetroxide, has been prepared (12). It is considered to be the anhydride of H_2SO_5 , Caro's acid, but reacts only slowly with water (4, p. 349). Sulphur tetroxide is a powerful oxidizing agent but is unstable toward heat, decomposing into sulphur trioxide and oxygen (4, p. 297). The intermediate formation of sulphur tetroxide would also explain the thermal decomposition of potassium persulphate in the absence of a solvent:



Also, it is quite possible that polymerizations catalyzed by persulphate may in reality be the result of initiation by oxygen atoms or sulphur tetroxide molecules, rather than by sulphate ion radicals ($\text{SO}_4^{\cdot-}$), as has been previously assumed (2, 5).

The reverse of Equations 7 and 12, the reaction of sulphur tetroxide with sulphate ion, may well constitute a new method for preparing persulphates (9, p. 108).

DERIVATION OF THE RATE EQUATION

A rate equation of the required form (cf. Eq. 1) may be derived from the proposed mechanism in the following manner.

In addition to the symbols P and S (defined above), let A represent the concentration of sulphate ion; B , that of the sulphur tetroxide; and X , that of the complex.

Applying the steady-state treatment to both B and X , one obtains

$$dB/dt = k_1P - k_2BS - k_{-1}AB + k_{-2}X = 0 \quad [13]$$

and

$$dX/dt = k_2BS - k_{-2}X - k_3X = 0. \quad [14]$$

Eliminating B from Equations 13 and 14, solving for X , and setting the over-all rate equal to k_3X , one obtains the final rate expression

$$-\frac{dP}{dt} = \frac{k_1SP}{S + Ak_{-1}\left(\frac{k_{-2} + k_3}{k_2k_3}\right)} \quad [15]$$

Using the original chemical notation this becomes

$$-\frac{d[\text{S}_2\text{O}_8^{2-}]}{dt} = \frac{k_1[\text{RSH}][\text{S}_2\text{O}_8^{2-}]}{[\text{RSH}] + [\text{SO}_4^{2-}]k_{-1}\left(\frac{k_{-2} + k_3}{k_2k_3}\right)} \quad [15a]$$

Hence, the observed rate constant, k , is evidently given by

$$k = \frac{k_1[\text{RSH}]}{[\text{RSH}] + [\text{SO}_4^{2-}]k_{-1}\left(\frac{k_{-2} + k_3}{k_2k_3}\right)} \quad [16]$$

Comparing Equation 16 with the empirical expression (Eq. 2), it is seen that

$$a = k_1 \quad [17]$$

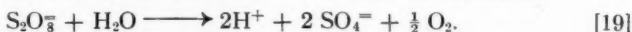
and

$$b = [\text{SO}_4^{2-}]k_{-1}\left(\frac{k_{-2} + k_3}{k_2k_3}\right). \quad [18]$$

The rate constant k_1 for the dissociation of persulphate ion into sulphur tetroxide and sulphate ion has, therefore, been determined in these experiments; and the activation energy (26 kcal. per mole) calculated from the value of the maximum rate constant (k_1) at different temperatures, does, indeed, appear to be the value to be associated with that reaction (3). Unfortunately, there are not sufficient data to allow an evaluation of any of the four other rate constants.

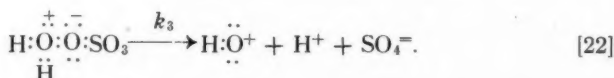
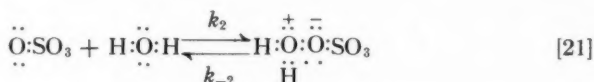
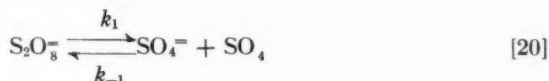
THE PERSULPHATE OXIDATION OF WATER

The molecular-ionic mechanism offered above can be applied with equal advantage to the decomposition of potassium persulphate in water, or, more exactly, the oxidation of water by persulphate. This reaction has been studied extensively (6, 8, 10). It may be represented by the over-all equation:



Previous mechanisms for this reaction have assumed either the intermediate formation of Caro's acid and hydrogen peroxide (10), or of sulphate ion radicals and hydroxyl radicals (HO^\bullet) (1).

The present mechanism includes none of these entities as necessary intermediates, though it allows for their possible formation in subsequent reactions. The new mechanism is:



The ion HO^+ , whose presence has been postulated in acidic aqueous hydrogen peroxide solutions (11), could then react in a number of ways, among which the most likely is probably:



If the complex formed in Equation 21 were to lose a proton, Caro's acid (HSO_5^-) would result.

The rate equation developed from Equations 20–22 in a manner quite analogous to the derivation presented for the oxidation of mercaptans is identical with Equation 15a, except that $[\text{H}_2\text{O}]$ replaces $[\text{RSH}]$. Thus:

$$-\frac{dP}{dt} = \frac{k_1[\text{H}_2\text{O}][\text{S}_2\text{O}_8^{2-}]}{[\text{H}_2\text{O}] + [\text{SO}_4^{\cdot -}]k_{-1}\left(\frac{k_{-2} + k_3}{k_2k_3}\right)} \quad [24]$$

The oxidation of water, however, proceeds much more slowly at a given temperature than the oxidation of mercaptans (3). The reaction of sulphur tetroxide with water is known to be slow (4, p. 349), and it is logical, therefore, to suppose that it is this reaction which retards the entire process. Equation 24 may be rearranged to:

$$-\frac{dP}{dt} = \frac{k_1k_2k_3[\text{H}_2\text{O}][\text{S}_2\text{O}_8^{2-}]}{k_2k_3[\text{H}_2\text{O}] + [\text{SO}_4^{\cdot -}]k_{-1}(k_{-2} + k_3)} \quad [25]$$

In this form it is more easily seen that if k_2 is very small, the first term in the denominator is small by comparison with the second term, and the retarding effect of sulphate is accentuated. Furthermore, the value of the numerator is lessened considerably by a small value for k_2 , and thus the rate of disappearance of persulphate is greatly diminished.

ACKNOWLEDGMENT

The author wishes to thank Dr. C. A. Winkler for his kindness in furnishing the data for Tables I and II, which heretofore had not been published.

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REACTIONS OF CYANOGEN IODIDE¹

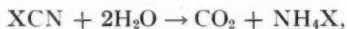
By L. E. BODNAR² AND A. B. VAN CLEAVE

ABSTRACT

A series of hydrogen chloride catalyzed reactions involving cyanogen iodide as the starting material have been investigated in dioxane and in aqueous solution at 30° and 45° C. The course of the reaction was followed by determining the decrease in the number of oxidation equivalents present. Reaction products identified were: iodine monochloride, iodine, ammonium chloride, and carbon dioxide. A possible reaction mechanism has been suggested.

INTRODUCTION

A previous study (18) of the reaction between cyanogen chloride and water and between cyanogen bromide and water, catalyzed by hydrogen chloride or hydrogen bromide in dioxane solution, has established that the over-all reaction is represented by



where X represents chlorine or bromine. In both cases the catalyst was indicated to be molecular hydrogen chloride or hydrogen bromide rather than hydronium ions. It is of interest to study the hydrolysis of cyanogen iodide under conditions similar to those employed for the other cyanogen halides. The present work indicates that the reactions undergone by cyanogen iodide are quite different from those of either cyanogen chloride or cyanogen bromide.

EXPERIMENTAL

1. Chemicals

(a) Cyanogen iodide was prepared from potassium cyanide and iodine according to the method of Comastri (3). A yield of about 66% was obtained by thoroughly cooling vessels and reagents before use. Two purifications by sublimation were necessary to remove traces of iodine.

(b) Dioxane (Eastman Kodak) was purified by the method of Fieser (4) and was distilled from metallic sodium just before use.

(c) Alcohols: methanol and ethanol were dried by refluxing with magnesium turnings.

(d) Ammonium iodide (Merck) was dried over phosphorus pentoxide and stored in the dark.

(e) Solutions of hydrogen chloride in dioxane were prepared either by adding appropriate amounts of concentrated C.P. hydrochloric acid or by bubbling pure dry hydrogen chloride into anhydrous dioxane. Solutions prepared by the latter method were analyzed over a period of time to determine whether there were any reactions corresponding to that observed for

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solutions of hydrogen bromide in dioxane (17). Over a period of three weeks at 45° C., no detectable decrease in the concentration of hydrogen chloride in a 0.425 *M* solution was observed.

(f) Iodine monochloride was prepared by passing chlorine into solid iodine until the mass became liquid and then fractionating twice to remove iodine and iodine trichloride (2).

2. Procedure

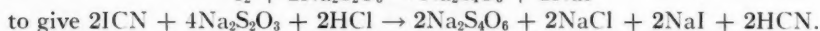
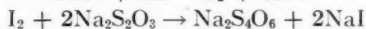
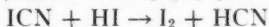
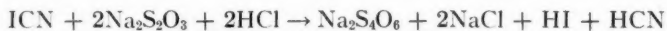
A definite amount of solid cyanogen iodide was weighed into a 100 ml. volumetric flask, the desired amount of distilled water added, and the volume made up to 100 ml. with anhydrous dioxane containing known amounts of dry hydrogen chloride. After mixing, 10 ml. aliquots of the solution were transferred to glass reaction tubes which were cooled in ice water. The tubes were then quickly sealed with a torch and placed in a constant temperature bath. Individual tubes were opened for analysis at appropriate times using a hot wire glass cutter. The same general procedure was used in experiments with solvents other than dioxane.

3. Analytical Methods

In studying the reaction between cyanogen chloride or cyanogen bromide and water in dioxane solution, it was established that the solubility of the ammonium halide formed was low enough to permit rate studies by determining the amount of precipitated ammonium halide (18). Preliminary experiments on the solubility of ammonium iodide in dioxane-water solution at 25° C. indicated, however, that its solubility was too high for this method to be applicable to cyanogen iodide reactions. Consequently, a method based on the determination of the concentration of oxidizing agents in the solution was adopted.

A. Determination of Cyanogen Iodide

(1) Cyanogen iodide in dioxane or other solvent was added to 150 ml. of water containing 10 ml. of 6 *N* hydrochloric acid and titrated with standard sodium thiosulphate solution using starch as an indicator.* According to Meineke (9), the sequence of reactions is as follows:



(2) The above method was modified by the addition of an excess of potassium iodide just before the titration. This resulted in the immediate liberation of iodine which was titrated with standard thiosulphate solution. With weighed samples of cyanogen iodide, quantitative recovery and good agreement

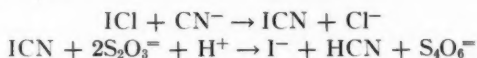
* The blue color formed by starch and iodine does not appear in aqueous solutions which contain more than about 27% by volume of dioxane. In the region of 27% by volume of dioxane, the complex is brown and in solutions more concentrated in dioxane there is no color at all. A sufficiently large concentration of alcohol also prevents the formation of the blue starch-iodine color.

was obtained by either A(1) or A(2). In agreement with the results of Meineke (9) the reaction between cyanogen iodide and sodium thiosulphate in neutral solution was found to be incomplete.

B. Determination of Iodine Monochloride

(1) Since iodine monochloride was identified as a reaction product (Section 4), it was necessary to study its reaction with sodium thiosulphate. A direct titration in hydrochloric acid solution indicated that the reaction was incomplete and variable as reported by Lang (8).

(2) Following the method of Lang (8), iodine monochloride in dilute hydrochloric acid was added to 150 ml. of water containing 10 ml. of 6 *N* hydrochloric acid. Five grams of sodium acetate was added, followed by sufficient potassium cyanide to decolorize the solution. The reactions,



were found to be quantitative.

(3) Instead of adding sodium acetate and potassium cyanide as in (2) above, an excess of potassium iodide was added just before titration with thiosulphate solution. Iodine was liberated immediately by the reaction, $\text{ICl} + \text{KI} \rightarrow \text{KCl} + \text{I}_2$. Quantitative agreement was obtained between methods B (2) and B (3).

C. Determination of Cyanogen Iodide, Iodine Monochloride, and Iodine

No successful method was devised for determining both cyanogen iodide and iodine monochloride in the same solution. The total concentration of oxidation equivalents due to both was, however, determined by using the procedure outlined in A(2) or B(3) above. Furthermore, it was not found feasible to test for the presence or absence of iodine in iodine monochloride solutions. A solution of iodine monochloride in dilute hydrochloric acid gives a brown color with starch as does a solution of iodine and iodine monochloride. Although iodine monochloride is insoluble in chloroform, the chloroform test for iodine also fails, as the addition of iodine monochloride solution to a solution of iodine in chloroform results in the chloroform layer becoming colorless with no apparent change in the yellow hydrochloric acid layer.

It is possible to determine iodine in the presence of cyanogen iodide by precipitation of the former with silver nitrate. However, in the present experiments the situation was complicated by the presence of a relatively large amount of hydrochloric acid, which precipitated silver chloride along with any silver iodide that might form. When known amounts of cyanogen iodide containing hydrochloric acid were treated with varying amounts of silver nitrate solution and then titrated with sodium thiosulphate solution, it was observed that the apparent number of oxidation equivalents present decreased as the amount of silver nitrate present increased. This was probably due to some of the iodine, formed in the titration reaction, exchanging with chlorine in the silver chloride precipitate. It was concluded that it was not possible to analyze mixtures of cyanogen iodide and iodine quantitatively in the presence of hydrochloric acid by this method.

A preliminary attempt was made to determine whether cyanogen iodide, iodine monochloride, and iodine could be distinguished in solution with a Beckman Model DU spectrophotometer. It was found that the solutions used in this work would have to be diluted many times to give readings on the instrument and that the results might not, therefore, be reliable. Furthermore, there appears to be considerable disagreement in the literature as to the positions of the absorption maxima for iodine. Also, the absorption maximum for iodine monochloride in solvents giving yellow solutions is reported (5) to coincide with an absorption maximum for iodine solutions. In view of these difficulties the search for a spectrophotometric method was abandoned.

Since no simple method of distinguishing between cyanogen iodide, iodine monochloride, and iodine was apparent, a method, A(2) or B(3), above, which determined only the total number of oxidation equivalents present was adopted.

4. Identification of Reaction Products

A. Ammonium Chloride

What appeared to be a mixture of crystals eventually appeared in most of the experiments conducted in dioxane solution. The bulk of these crystals had a yellow color but, mixed with this, there was always a smaller amount of a white crystalline material. In experiments where the initial molar ratio of water to cyanogen iodide was greater than 2:1, only the white crystals formed. A quantity of these crystals, recovered after six weeks from an experiment in which the initial molar ratio of water to cyanogen iodide was 4:1 and the initial hydrogen chloride concentration, 2.61 *M* gave a positive test for chloride and, on Kjeldahl analysis, 96.52% of the theoretical ammonia for ammonium chloride. (This compares with a 98.07% recovery of ammonia from a sample of pure ammonium chloride by the same procedure.) In another experiment, when the initial water to cyanogen iodide ratio was 10:1, and the initial hydrogen chloride concentration 1.302 *M*, the white crystals were quantitatively recovered after one month. Their dry weight was 0.0810 gm., while the theoretical amount of ammonium chloride corresponding to complete conversion of the nitrogen in the cyanogen iodide was 0.0805 gm. The solubility of ammonium chloride in a dioxane-water solution of the concentration involved in this experiment was negligible (18). On the basis of these experiments it was concluded that ammonium chloride was quantitatively produced when more than the stoichiometric amount of water was present in the reaction mixture. Ammonium chloride was also positively identified in experiments where butanol was used as a solvent in place of dioxane.

The yellow crystalline material produced in all experiments in dioxane where the initial hydrogen chloride concentration was from 0.12 to 1.647 *M* and where the initial molar ratio of water to cyanogen iodide was not greater than 2:1, was not definitely identified. This material was not very stable on exposure to the atmosphere and was believed to be a molecular compound of dioxane and ammonium iodide or iodine or iodine monochloride (15, 16).

B. Iodine Monochloride and Iodine

It was observed that a brown coloration invariably appeared after a time in the reaction tubes. This coloration was first established as being due to iodine monochloride in an experiment with methanol as the solvent. In this particular case, a bright yellow color was produced immediately on adding 25 ml. of methanol, which was 7.71 *M* in hydrogen chloride, to 0.625 gm. of cyanogen iodide and 0.147 ml. of water. The solution darkened with time to a reddish color. A portion of this solution, after dilution with dilute hydrochloric acid and the addition of starch solution showed the brown color characteristic of iodine monochloride (8). This brown color changed to blue when potassium iodide was added, presumably owing to the reaction, $\text{ICl} + \text{KI} \rightarrow \text{KCl} + \text{I}_2$. Also, when a second portion of this reddish colored methanol solution was treated with sodium acetate followed by potassium cyanide, it was completely decolorized. The reaction would be (6), $\text{ICl} + \text{KCN} \rightarrow \text{ICN} + \text{KCl}$.

As an additional test, two equal portions of the methanol solution were diluted to five times their original volume, one with water and the other with dilute hydrochloric acid. The color darkened and iodine crystals separated from the water diluted solution in a few hours, owing to the reaction (12), $5\text{ICl} + 3\text{H}_2\text{O} \rightarrow \text{HIO}_3 + 5\text{HCl} + 2\text{I}_2$. There was no apparent change in the solution diluted with hydrochloric acid on standing over night. All of the above results are in accord with the known reactions of iodine monochloride.

Numerous similar tests were carried out for experiments in which dioxane was the solvent and, in all except one case, the brownish coloration appeared to be due to iodine monochloride. In the one exception, a positive test for iodine rather than iodine monochloride was obtained, but this was in an experiment that had been allowed to run to completion (about two weeks) and in which the iodine from the cyanogen iodide (or iodine monochloride) had been reduced to elementary iodine.

The appearance of iodine crystals was also noted in experiments conducted in aqueous solution after they had been in progress for a considerable time. This would be expected from the reaction between iodine monochloride and water indicated above.

C. Carbon Dioxide

Carbon dioxide was identified as a reaction product in cases where cyanogen iodide was allowed to react with hydrogen chloride in aqueous solution. However, no positive test for carbon dioxide was obtained for reactions in dioxane, although considerable gas pressure was noted in some tubes in which the reaction had proceeded for several days. Unfortunately, the literature does not appear to contain any information on the solubility of carbon dioxide in dioxane.

5. Results

A. The Rate of the Reaction between Cyanogen Iodide, Water, and Hydrogen Chloride in Various Solvents

Rate studies on the reaction between cyanogen iodide, water, and hydrogen chloride in aqueous solution and also in methanol, ethanol, and dioxane solutions at 45° C. were carried out by determining the change in the number

of equivalents of oxidizing agent present with time. As indicated above, the analytical method (Section 3 A(2)) adopted, did not distinguish between cyanogen iodide, iodine monochloride, or iodine. Typical results for these experiments are shown in Fig. 1. Except for the experiments in aqueous

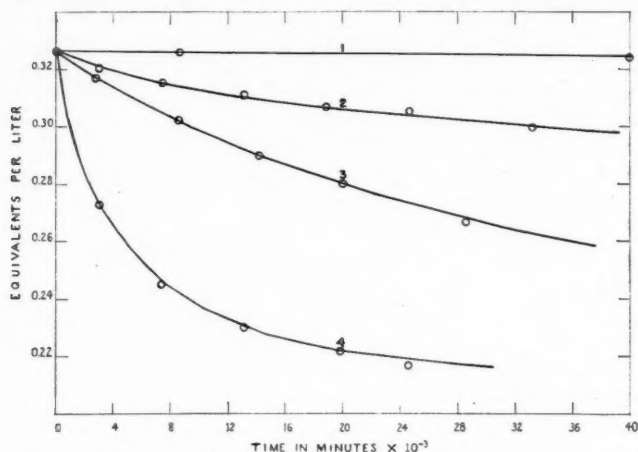


FIG. 1. The effect of solvent on the rate of reaction between cyanogen iodide, water, and hydrogen chloride.

1. Solvent, water, initial concentration of hydrogen chloride 0.233 *M*.
2. Solvent, methanol, initial concentration of hydrogen chloride 0.0916 *M*.
3. Solvent, ethanol, initial concentration of hydrogen chloride 0.0916 *M*.
4. Solvent, dioxane, initial concentration of hydrogen chloride 0.0916 *M*.

solution the initial molar ratio of water to cyanogen iodide was 2:1. It is to be noted that the rate of decrease of oxidation equivalents was much slower in water than in the other solvents, even though the initial concentration of hydrogen chloride was considerably greater. Since the polar nature of the solvents decreases in the order, water, methanol, ethanol, dioxane, it is to be expected that the degree of dissociation of the hydrogen chloride in these solvents will decrease in the same order. These experiments may, therefore, be taken as qualitative evidence that it is probably molecular hydrogen chloride that reacts with, or catalyses some reaction of, cyanogen iodide.

B. The Effect of Hydrogen Chloride Concentration on the Rate of Reaction between Cyanogen Iodide and Water in Dioxane Solution

A series of experiments at 45° C. was carried out in dioxane solution with initial concentrations of water and cyanogen iodide in the molar ratio of 2:1 and with initial hydrogen chloride concentrations varying from 0.125 *M* to 1.647 *M*. The results shown in Fig. 2 indicate that, although there was a relatively rapid initial decrease in oxidation equivalents at 45° C., the reaction eventually became very slow at a concentration level which was dependent on the initial concentration of hydrogen chloride. It is to be noted that the lower the initial hydrogen chloride concentration, the greater was the decrease in the number of oxidation equivalents per liter.

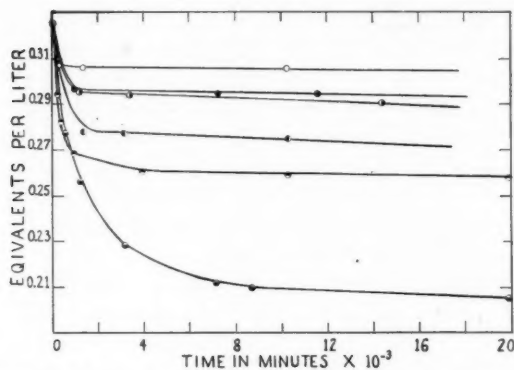


FIG. 2. The effect of hydrogen chloride concentration on the rate of reaction between cyanogen iodide and water in dioxane solution. Initial hydrogen chloride concentrations:

○ 1.647 *M* ● 0.991 *M* ● 0.491 *M*
 ● 1.302 *M* ● 0.656 *M* ● 0.126 *M*

Since the curves shown in Fig. 2 do not fit any simple rate equation, very approximate relative rates of reaction for the initial stages of the reaction were determined by drawing tangents to the concentration vs. time curves. Relative reaction rates evaluated in this way are shown plotted against the initial

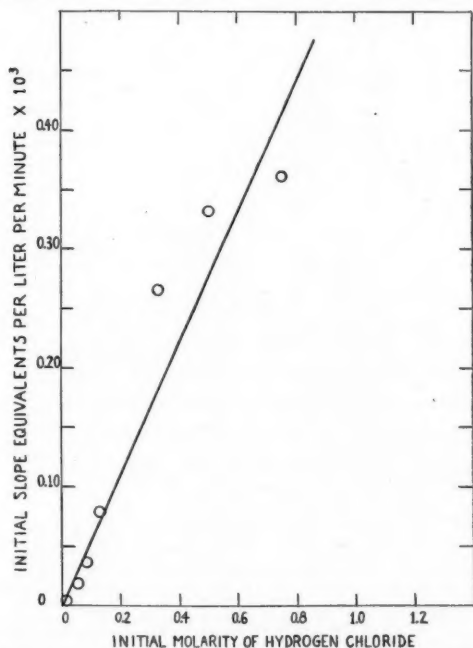


FIG. 3. The effect of hydrogen chloride concentration on the initial rate of reaction of cyanogen iodide with water in dioxane solution.

molarity of hydrogen chloride in Fig. 3. In the presence of the relatively small concentration of water employed in these experiments (about 0.32 moles per liter), most of the hydrogen chloride may be assumed to be in the molecular condition and therefore the initial reaction rate is approximately proportional to the concentration of molecular hydrogen chloride in the dioxane.

C. The Effect of Water Concentration on the Rate of the Reaction Between Cyanogen Iodide, Water, and Hydrogen Chloride in Dioxane Solution

Experiments at 45° C. in dioxane which was 1.302 M with respect to hydrogen chloride and with initial ratios of cyanogen iodide to water of 1:10, 1:4, 1:2, and 1:0, respectively, gave results as indicated in Fig. 4. The decrease

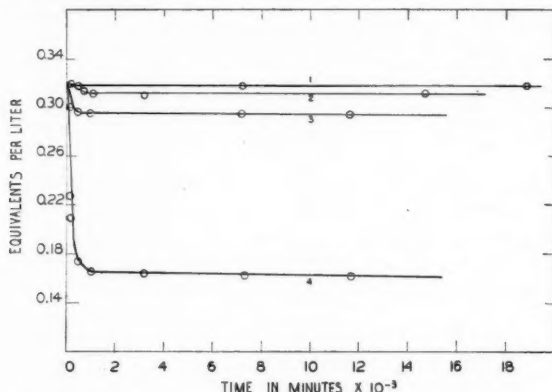


FIG. 4. The effect of water concentration on the rate of reaction between cyanogen iodide, water, and hydrogen chloride in dioxane solution. Initial concentrations of water: (1) 1.635 moles per liter; (2) 0.654 moles per liter; (3) 0.327 moles per liter; (4) 0.000.

in oxidation equivalents was most rapid in the case where no water was initially present and the higher the initial concentration of water the slower was the reaction and the smaller was the decrease in oxidation equivalents. The experiment with no water present was the only one in dioxane solution where the reaction apparently proceeded until all of the cyanogen iodide was converted to iodine, crystals of which were isolated. This result suggests that the cyanogen iodide was converted to iodine monochloride which, in turn, reacted with the dioxane with the eventual formation of iodine. Independent experiments established that solutions of cyanogen iodide in dioxane are reasonably stable and that iodine monochloride reacts with dioxane in the presence of hydrogen chloride.

D. The Effect of Cyanogen Iodide Concentration on the Rate of the Reaction between Cyanogen Iodide, Water, and Hydrogen Chloride in Dioxane Solution

In this series of experiments at 45° C. in dioxane, the initial concentrations of water and hydrogen chloride were kept constant at 0.327 and 0.324 moles per liter, respectively, while the initial concentration of cyanogen iodide was varied from 0.094 to 0.197 moles per liter. When the approximate initial slopes (as determined by drawing tangents) of the oxidation equivalents vs. time

curves were plotted against the initial cyanogen iodide concentration, a straight line relationship was obtained, indicating that, at least in the initial stages, the reaction is of the first order with respect to cyanogen iodide.

E. The Reaction Between Cyanogen Iodide, Water, and Hydrogen Chloride in Aqueous Solution

To avoid some of the complications indicated in the experiments where dioxane was used as the solvent, a series of experiments was carried out in aqueous hydrochloric acid solution. As was indicated by the results shown in Fig. 1, it was necessary to use considerably higher hydrogen chloride concentrations than in dioxane solution to obtain appreciable reaction rates. The initial rate of decrease of oxidation equivalents was found, as in dioxane solution, to increase with increasing initial hydrogen chloride concentration. Also, in the later stages of the reaction an almost stationary level, depending on the initial hydrogen chloride concentration, was reached in all cases except those where the initial hydrogen chloride concentration was below about 6 M. The results of a typical series of such experiments at 45° C. are shown in Fig. 5.

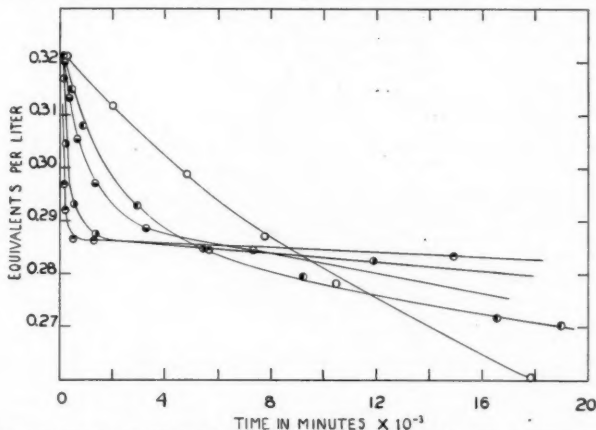


FIG. 5. The effect of hydrogen chloride concentration on the rate of reaction of cyanogen iodide with water in aqueous solution. Initial concentrations of hydrogen chloride:

- | | |
|-----------|-----------|
| ○ 5.735 M | ● 7.819 M |
| ● 6.631 M | ● 8.579 M |
| ◐ 7.064 M | |

Approximate initial rates for the decrease of oxidation equivalents at 45° C. were determined by drawing tangents to the concentration vs. time curves. When these initial rates were plotted against the calculated activity of hydrogen chloride (1), a linear relationship was indicated as shown by Fig. 6. A similar relationship was indicated by a few results obtained at 30° C. These results suggest that the concentration of molecular hydrogen chloride controls the initial reaction rate.

Although the initial rates of reaction were greater at 45° C. than at 30° C. (for the same initial concentrations of hydrogen chloride and cyanogen iodide), it was observed that the reaction at 30° C. proceeded more nearly to completion

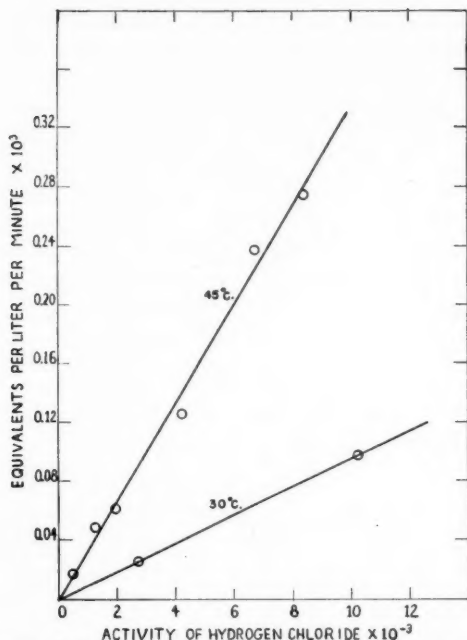
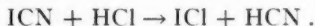


FIG. 6. Dependence of the initial rate of reaction between cyanogen iodide, water, and hydrogen chloride in aqueous solution on the activity of hydrogen chloride at 45° C. and 30° C.

before reaching the stage where the rate of decrease in oxidation equivalents became extremely slow. Assuming a first order reaction, the apparent activation energy for the initial reaction in 7 to 8 *M* hydrogen chloride was calculated to be about 8000 calories per mole.

F. *The Reaction of Formic Acid with Iodine Monochloride in the Presence of Hydrogen Chloride*

As shown above, iodine monochloride was produced in the reaction mixtures, probably by the reaction:



The hydrolysis of hydrogen cyanide in acid solutions has been studied (6, 7, 13, 14) and shown to proceed through the stages:



Free energy calculations indicated that a reaction between iodine monochloride and formic acid was possible and consequently a few experiments were carried out to study this reaction.

The results of an experiment at 45° C. in 5.9 *M* hydrochloric acid with initial concentrations of formic acid and iodine monochloride, 2.210 and 0.446 moles per liter, respectively, are shown in Fig. 7. The analytical method employed was the same as that used in the cyanogen iodide experiments. In this

case, however, iodine and iodine monochloride are the only oxidizing agents present that react with thiosulphate and the concentration of both could be calculated from one titration value. The reason for this is that, when the reaction of iodine monochloride and formic acid is complete, that is, all the iodine monochloride converted to iodine, one half of the original number of oxidation equivalents remain.

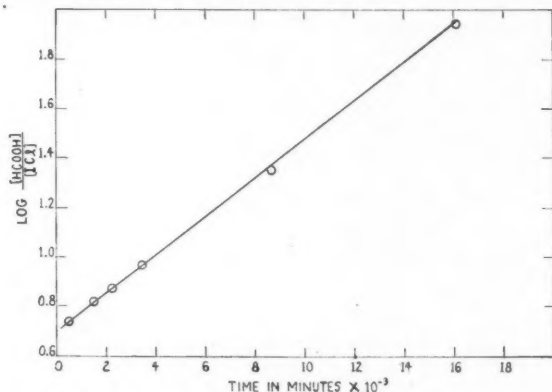
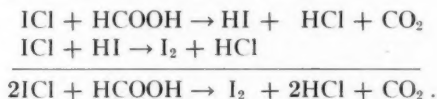


FIG. 7. Data for the reaction between formic acid and iodine monochloride, at 45° C., plotted on the basis of a bimolecular reaction.

Since no direct determination of the formic acid concentration was made, it was assumed that its rate of decrease was one half that shown by iodine monochloride, in accordance with the reactions:



Further, if it is assumed that the first of these reactions is rate determining and bimolecular (the second reaction is known to be very fast (10)), the plot of $\log [\text{HCOOH}]/[\text{ICl}]$ vs. time, should give a straight line relationship as observed in Fig. 7 to as high as 95% completion of the reaction. The average specific rate constant for this experiment was, $k = 4.7 \times 10^{-5}$ liters/mole/minute.

Some preliminary work was done on the effect of the hydrogen chloride concentration on the rate of the reaction between formic acid and iodine monochloride at 45° C. In these experiments the initial molar ratio of formic acid to iodine monochloride was approximately 1:1, with actual concentrations of the same order as would be produced in the cyanogen iodide experiments, that is, about 0.09 molar. Treating the data as indicated above, average specific rate constants of $k = 5.5 \times 10^{-5}$ liters/mole/minute, and $k = 1.4 \times 10^{-5}$ liters/mole/minute, were obtained for initial hydrochloric acid molarities of 5.86 and 7.87, respectively. That is, other factors being constant, the rate of reaction between formic acid and iodine monochloride decreases with

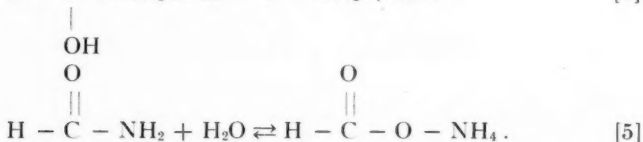
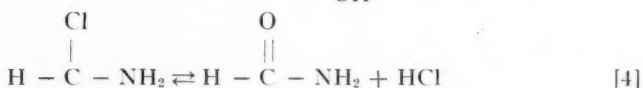
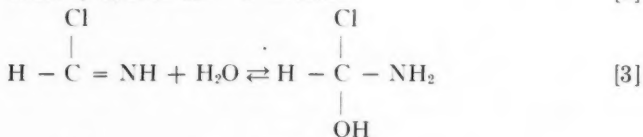
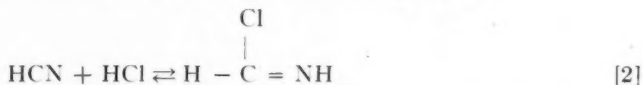
increasing concentration of hydrogen chloride. This effect could possibly be due to a reversal of the suggested reactions but, since a constant rate was observed to 95% reaction of the iodine monochloride, this does not seem likely. It is more probable that the change in rate was a result of change in environment (11). In any case, these experiments indicated that the rate of reaction between formic acid and iodine monochloride was too slow to account for the observed rate of decrease in oxidation equivalents in the initial stages of the cyanogen iodide experiments.

DISCUSSION

The formation of iodine monochloride indicates that the primary step in the reaction of cyanogen iodide with hydrogen chloride and water in either dioxane or aqueous solution is probably:



The hydrolysis of hydrogen cyanide in aqueous hydrochloric acid proceeds, according to Krieble and McNally (6), by the following steps:

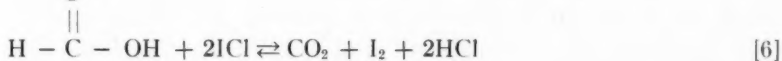
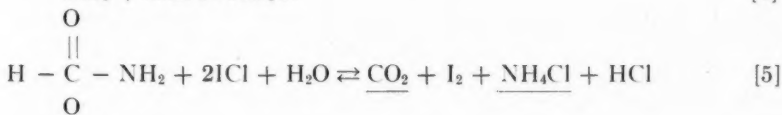
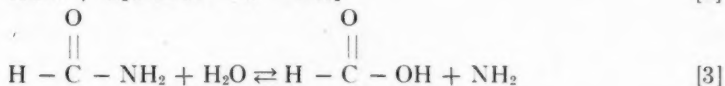
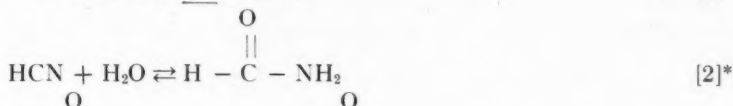


They suggested that reactions [5] and [4] were very fast compared to [2] and that the second hydrolysis, represented by [5] was faster than [3]. They also concluded that molecular hydrogen chloride was the effective catalyst. Krieble and Peiker (7) continued this study and concluded that the rate of hydrolysis of hydrogen cyanide was independent of its concentration.

Rabinovitch and Winkler (13, 14) have studied the hydrogen chloride catalyzed hydrolysis of formamide and hydrogen cyanide. They observed a maximum in the rate of hydrolysis of formamide in 4-6 *N* acid which they interpreted as being due to a maximum concentration of an amide cation. The relative rate ratios for the hydrolysis of the nitrile and amide were found to vary from 1:12,000 in 1.00 *N* acid to 1:3 in 8.47 *N* acid.

On the basis of these results obtained by previous authors and the information provided by the present work, it seems probable that the following series

of reactions occur in aqueous hydrochloric acid solutions of cyanogen iodide: (reaction products definitely identified in this work are underlined).



To account for the reduction of the iodine in iodine monochloride, either the formamide and/or the formic acid, produced in reactions [2] and [3], must be oxidized. The preliminary study made of the oxidation of formic acid by iodine monochloride indicated that reaction [6] was not nearly rapid enough, under the conditions of these experiments, to account for the relatively rapid initial rate of reaction observed in both aqueous and dioxane solutions. It therefore appears necessary to postulate that the relatively rapid initial rate of decrease in oxidation equivalents is due to the oxidation of formamide by iodine monochloride as represented by equation [5]. Unfortunately, no information on this reaction is available. Since, at least in the initial stages, the rate of decrease of oxidation equivalents was found to be proportional to the activity of the undissociated hydrogen chloride (Fig. 6) it is suggested that reaction [1] is initially the rate controlling process.

Assuming that reaction [5] does occur at a more rapid rate than reaction [6], it is possible to account for the levelling off of the oxidation equivalent vs. time curves as shown in Figs. 2 and 5, as follows: The primary hydrolysis of hydrogen cyanide (reaction [2]) occurs at a rate which increases by a factor of 1000 on increasing the hydrogen chloride concentration from 1.95 *M* to 7.84 *M* (6), while the hydrolysis of formamide (reaction [3]) occurs at a rate which increases with increasing hydrogen chloride concentration, reaching a maximum in about 4 *M* acid, and then decreasing to one half the maximum value when the hydrogen chloride concentration is increased to about 8 *M* (13). In several of the present experiments the amount of ammonium chloride recovered corresponded to total conversion of the nitrogen in the cyanogen iodide, that is, to complete hydrolysis of the hydrogen cyanide formed in reaction (1).

* Probably as a series of reactions as suggested by Krieble and McNally (8), whose results indicate that the rate of reaction [2] under comparable conditions, is considerably greater than the initial rate of decrease of oxidation equivalents observed in the present work.

At the same time, however, the reaction as measured by the decrease in oxidation equivalents was not nearly complete. If the formamide reacts both by hydrolysis (reaction [3]) and by oxidation (reaction [5]) and if the relative rates of these two reactions change with a change in the hydrogen chloride concentration, the initial relatively rapid rate of decrease of oxidation equivalents in solutions of high hydrogen chloride concentration could be accounted for in terms of higher iodine monochloride and formamide concentrations than are present in solutions of lower hydrogen chloride concentration. The greater degree of completion of the reaction (as measured by oxidation equivalents) in solutions of lower hydrogen chloride concentration may be explained by assuming that relatively more formamide is oxidized by iodine monochloride (reaction [5]) before complete hydrolysis of the formamide occurs (reaction [3]). As soon as all the formamide has been used up, both by hydrolysis and oxidation, the rate of decrease of oxidation equivalents becomes very small, as the oxidation of formic acid by iodine monochloride (reaction [6]) has been shown to be very slow under the experimental conditions. This could cause the virtual levelling off of the oxidation equivalent vs. time curves as observed.

When dioxane was used as the solvent it is probable that the same reactions occurred along with complications involving reactions of dioxane with cyanogen iodide, iodine monochloride, and iodine, to form molecular compounds.

ACKNOWLEDGMENT

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THE THERMAL DECOMPOSITION OF *n*-BUTANE¹

By V. A. CRAWFORD² AND E. W. R. STEACIE

ABSTRACT

The thermal decomposition of *n*-butane at 442°C. has been investigated analytically in the pressure range 4–13 cm. Up to 9% decomposition, the rates of formation of H₂, CH₄, C₂H₄, and C₂H₆ are independent of time; the dependence of the rates on butane pressure was approximately first order. The validity of the extrapolation procedure for obtaining the initial products was established, there being no significant variation in the composition of the products with extent of decomposition. In the nitric oxide fully inhibited reaction irreproducible rate data were obtained although the proportions in which the products are formed seemed to be roughly invariable. In view of this it is suggested that no very definite conclusions can be drawn from a comparison of the composition of the products of the normal and fully inhibited reactions. The heterogeneity of the fully inhibited reaction is stressed for the importance of this has not hitherto been sufficiently recognized. Attention is drawn to the apparent inefficiency of nitric oxide as an inhibitor.

The thermal decomposition of paraffin hydrocarbons has been abundantly studied in the past, resulting in the establishment of certain general characteristics of such reactions. Nevertheless, certain salient features of the pyrolysis of the paraffins still remain to be elucidated.

In order to identify the initial products, recourse is usually had to a procedure which involves extrapolation of the products formed at real conditions to their values at zero decomposition (9). Although it is possible in principle to decrease the extent of decomposition until primary products only are formed, excessive dilution of the products with undecomposed paraffin presents a formidable analytical problem. Because of this, pyrolyses at fairly high pressures were carried to extents of decomposition ranging from 20–50% and the results extrapolated to zero decomposition. In order to obtain the initial products, therefore, an unduly large extrapolation is involved and in order to test its validity the range 0–20% requires exploration. The less laborious and more exact methods of analysis which are now available enable this to be done with reasonable facility.

The decomposition of paraffin hydrocarbons with two to eight carbon atoms has been explained as being in part a chain reaction involving free radicals. Evidence for this comes not only from the sensitized decompositions (10, 3) but also from the nitric oxide inhibition from which mean chain lengths from 2 to 20 may be calculated. These latter values are calculated on the assumption that the fully inhibited reaction is a molecular rearrangement and not a free radical process. This hypothesis would seem to be reinforced by the fact that, although nitric oxide is much more efficient than propylene, both inhibitors reduce the rates to the same limiting value.

The reaction, however, is not stopped in the presence of nitric oxide but merely slowed down and after 20–25% decomposition the inhibited rate is

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identical with the uninhibited. Initial rates therefore provide the only reliable criterion of the extent of inhibition. Moreover, as was first shown by Dintzes and Frost (1) and more recently conclusively demonstrated by Stubbs and Hinshelwood (13) the sigmoid nature of the $\Delta p - t$ curves for the higher paraffins is due to self inhibition by the products of the reaction. When studied at large conversions, therefore, the artificial nitric oxide inhibition reaction is being investigated under conditions rendered complicated by the self inhibition of the products. The desirability of investigating the nitric oxide inhibited reaction at small conversions is evident.

That the minimal inhibited rate corresponds to a pure molecular rearrangement, that is to a complete suppression of chains, is doubted by Steacie and Folkins for two reasons. (1) From a study of the free radical induced decomposition of butane they concluded that there is a certain fraction of residual chain decomposition at all concentrations of nitric oxide. (2) The products of the inhibited reaction were found to be the same as those of the normal reaction. With regard to (2) it may be noted that whether the ratio of chain reaction to molecular rearrangement is 100 : 1 or 1 : 1 depends on the differences between the activation energies and entropies of the alternate reaction paths. On this basis Hinshelwood (4) has recently shown that it is quite possible for the products from the molecular process and chain reaction to be in the same proportions. Unfortunately, the results of Steacie and Folkins, and Hinshelwood *et al.*, are not as conclusive as they might be for the work was done at too high conversions.

In some studies it has been reported that nitric oxide is used up during the inhibition, whereas other workers maintain that the inhibitor is only gradually consumed, if at all.

There are still therefore several problems connected with the pyrolysis of paraffin hydrocarbons. In order to obtain unequivocal results which may be discussed with assurance, it is essential that both the normal and the inhibited reactions be studied at small extents of decomposition. The results of such an investigation are reported here, and because of its intermediate complexity butane was chosen for this work.

MATERIALS

Butane which was obtained in cylinders from the Phillips Petroleum Company (Research grade) was stated to be 99.8% pure and was used without further purification except for bulb to bulb distillation and rigorous degassing.

Nitric oxide was obtained in cylinders from the Matheson Company. Its purity was stated to be not less than 98.7%, the balance being nitrogen and higher oxides of nitrogen. Consequently, the gas from the cylinder was passed through a trap at -120°C . to remove NO_2 and then into a storage bulb. It was condensed and distilled under vacuum in order further to ensure its purity.

APPARATUS AND PROCEDURE

Since the pyrolysis was to be carried to only small extents of decomposition, the reaction was studied at temperatures where it proceeds slowly. Further-

more, in order to ensure that sufficient products were available for accurate analysis, experiments were carried out in a static system using a large quartz reaction vessel which was about 12 in. long and 6 in. in diameter. It was contained in a furnace built of a steel tube 37 in. long, wound with 12 gauge Chromel A wire, and mounted vertically in a rectangular transite box lagged with asbestos fiber. Uniformity of temperature along the tube was achieved by winding the furnace in two sections. Three leads were brought out of the insulating box, one of which was a center tap common to each winding. Current for each winding was taken through a 20 amp. variac transformer from a 3 kva. Sorenson constant voltage regulator. The reaction vessel was mounted vertically in the center of the furnace and rested on a narrow transite ledge which was supported by a steel tube resting on the base of the furnace. The ends of the latter were closed by 5/16 in. boiler plate at the bottom and a tight fitting refractory plug at the top which contained holes for the reaction vessel outlet tube and thermocouples. By manual regulation it was possible to keep the temperature along the length of the vessel uniform to within 1–2°C. Temperatures were measured by using three chromel-alumel thermocouples. These were in contact with the outer surface of the reaction vessel and were situated at its base, center, and shoulder respectively. In addition, two variable thermocouples were available to explore the temperature variation along the whole length of the furnace. All thermocouples were calibrated in the temperature range to be used so the absolute values of the temperature should be accurate to $\pm 1^\circ\text{C}$. The results reported have been obtained at 442°C.

The reaction system comprised the reaction vessel, mercury manometer, traps, and bulbs for the purification of gases and a 5-liter sharing bulb. The gas analysis system consisted of a sampling bulb, liquid nitrogen traps, mercury diffusion pump, a low temperature still similar to that described by LeRoy (5), a McLeod gauge, and combined Toepler pump and gas burette.

Each experiment was conducted by admitting a known pressure of butane to the sharing bulb and then expanding the gas for 10 sec. into the reaction vessel at which instant the sharing bulb was isolated. After the reaction had proceeded the desired length of time, samples of the reaction products for analysis were obtained by allowing the gases in the reaction vessel to expand for 10 sec. into an evacuated 1-liter sampling bulb at room temperature. Here the reaction products together with unchanged butane were frozen out in liquid nitrogen and the hydrogen and methane pumped off. Blank experiments showed that both these gases are removed quantitatively by repeated cycles of freezing, pumping, and evaporating. After removal of the noncondensables, the residue in the sampling bulb was condensed into the Ward still. Blank experiments showed a 100% recovery of small amounts of ethylene and ethane mixed with a large amount of butane (1 : 200). Unfortunately, however, it was not found possible to recover propylene quantitatively from a large excess of butane and hence propylene was not analyzed for. This is perhaps a disadvantage of the present work, but if it is agreed that it is important to study the initial stages of the reaction, then this is almost inevitable. Ward still analysis

separated the C_2 fraction from higher hydrocarbons and the former by mass spectrometer analysis was found to consist only of C_2H_6 and C_2H_4 .

When the decomposition of butane in the presence of nitric oxide was studied, the nitric oxide was usually introduced into the reaction vessel just prior to the admission of butane. In some experiments, runs were made with mixtures of butane and nitric oxide which had been allowed to mix thoroughly before introduction to the reaction vessel. Within the rather large experimental error, no differences in the results were observed.

A sample for analysis was obtained in exactly the same manner as previously. The sampling bulb was cooled in liquid nitrogen and the noncondensables (H_2 , CH_4 , and NO) pumped off with the aid of the mercury diffusion pump and the pump down trap. By repeated cycles of freezing, pumping, and warming, it was possible to remove the NO completely from the sample. The residue in the sampling bulb was then condensed in the Ward still and the C_2 fraction obtained as before. Complete removal of NO from the C_2 fraction was always tested for by exposing it to an alkaline bead of sodium sulphite. The necessity for this procedure became apparent when it was found that nitric oxide on admission to the mass spectrometer gave the nitrogen m/e 28 peak the intensity of which was dependent on the pressure of nitric oxide. In the mass spectrometer, therefore, N_2 presumably arises from a bimolecular process involving nitric oxide. Furthermore, since NO and C_2H_6 have the same mass numbers there is perhaps some opportunity for confusion in their determination when they are present simultaneously. It was thought advisable, therefore, to separate the products not only from the large excess of unchanged butane but also from the nitric oxide. Indeed one of the distinguishing features of the present work is the very great care that has been taken to ensure that the C_2 fractions were uncontaminated with NO .

RESULTS

Because of technical difficulties, only H_2 , CH_4 , C_2H_4 , and C_2H_6 were analyzed for quantitatively. The effect of time on the production of these gases at $442^\circ C$. in the absence of nitric oxide is shown in Figs. 1, 2, 3, and 4. It is evident that the formation of all four gases varies linearly with time up to a time of decomposition of 30 min., that is from 1.5 to 9% conversion. The initial rates of

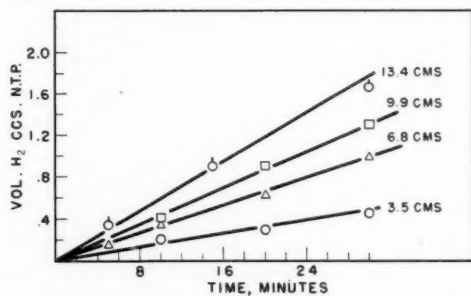


FIG. 1. Dependence of hydrogen formation on time and pressure of butane.

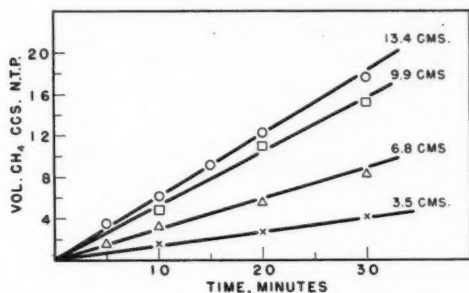


FIG. 2. Dependence of methane formation on time and pressure of butane.

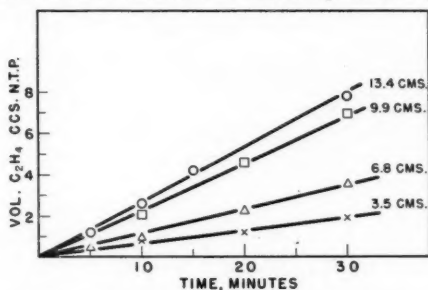


FIG. 3. Dependence of ethylene formation on time and pressure of butane.

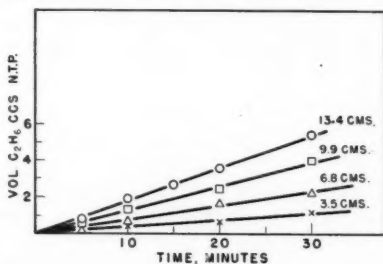


FIG. 4. Dependence of ethane formation on time and pressure of butane.

formation can therefore be determined unambiguously. It was found that at extents of decomposition greater than 10% there is a marked falling off from the linear relationship between formation of products and time. Stubbs and Hinshelwood (13) proved quite conclusively that the falling off in rate was due to inhibition by the products of the reaction. Since Rice and Polly (8) have shown that ethylene causes no detectable inhibition, the effect must be due largely to propylene.

A plot of the percentage products versus percentage decomposition was found to be linear up to 24% conversion. The extent of decomposition was computed from the pressure increase because technical difficulties made it impossible to determine the consumption of butane. This procedure is quite sound for whichever method is used it will correctly show the variation, if any,

in the composition of the products with extent of decomposition. There was no significant variation in the products with changes in the initial pressure over the range 4–13 cm. This agrees with the earlier work of Steacie and Puddington (12) who found that varying the initial pressure of butane from 20–60 cm. produced no noticeable change in the relative proportions of the products.

Inhibited Decompositions

It is well known that the rate of decomposition of butane is reduced by small additions of nitric oxide while, in the presence of a sufficient quantity of the inhibitor, the rate is reduced to a well defined limiting minimum value. The inhibited decompositions were studied under conditions identical with that of the normal decomposition except that the butane was pyrolyzed in the presence of $\frac{1}{10}$ th its pressure of nitric oxide, a value which is known to give maximum inhibition.

Unlike the normal decomposition where the rates of formation of the products were reproducible to within 2–5% it was now found impossible to obtain reproducible rate data. An example of this irreproducibility is shown in Table I which records the results of experiments carried out under identical conditions.

TABLE I

| Duration of run, min. | Volume of products generated in cc. N.T.P. | | | | P_{Butane} , cm. | P_{NO} , cm. |
|-----------------------|--|----------------|-------------------------------|-------------------------------|---------------------------|-----------------------|
| | CH ₄ | H ₂ | C ₂ H ₄ | C ₂ H ₆ | | |
| 5 | 0.91 | 0.055 | 0.16 | 0.066 | 13.24 | 1.50 |
| 5 | 0.93 | 0.072 | 0.20 | Absent | 13.19 | 1.41 |
| 5 | 0.88 | 0.076 | 0.40 | Absent | 13.14 | 1.43 |
| 5 | 1.69 | 0.103 | 0.44 | Absent | 13.60 | 2.08 |
| 5 | 0.62 | 0.048 | 0.30 | 0.022 | 13.84 | 1.33 |
| { 30 min. | 2.705 | 0.173 | 0.98 | 0.074 | 13.64 | 2.03 |
| { per 5 min. | 0.45 | 0.029 | 0.16 | 0.012 | | |

This may be accounted for in two ways. The mass spectrometer analyses of the very small quantities of products are not as accurate as may be desired. Secondly, and more important, the scatter in results may be a manifestation of the slight disturbance also noted by Stubbs and Hinshelwood (13) in the initial stages of the fully inhibited reaction.

TABLE II

| Extent of decomposition, % | % Composition of the products | | | | P_{Butane} , cm. | P_{NO} , cm. |
|----------------------------|-------------------------------|----------------|-------------------------------|-------------------------------|---------------------------|-----------------------|
| | CH ₄ | H ₂ | C ₂ H ₄ | C ₂ H ₆ | | |
| 0.96 | 75.7 | 4.6 | 19.6 | Absent | 13.60 | 2.08 |
| 2.2 | 68.9 | 4.4 | 24.5 | 1.9 | 13.64 | 2.03 |
| 0.98 | 76.3 | 4.6 | 13.5 | 5.6 | 13.24 | 1.50 |
| 0.98 | 77.1 | 5.9 | 16.9 | Absent | 13.19 | 1.41 |
| 0.91 | 65.1 | 5.6 | 29.3 | Absent | 13.14 | 1.43 |
| 0.95 | 62.6 | 4.8 | 30.3 | 2.2 | 13.84 | 1.33 |
| | 58 | 5 | 24 | 12 | | |

Table II gives the composition of the products resulting from the fully inhibited decomposition.

For comparison, the initial products of the normal decomposition are given in the bottom line of the table.

A few experiments were also made to determine the dependence of the rate of formation of C_2H_4 and C_2H_6 on the pressure of butane. The results obtained are given in Table III.

TABLE III

| Extent of decomposition, % | P_{Butane} , cm. | P_{NO} , cm. | cc. N.T.P. | | Duration of run, min. |
|----------------------------|---------------------------|-----------------------|------------|----------|-----------------------|
| | | | C_2H_4 | C_2H_6 | |
| 6.8 | 55.88 | 7.2 | 9.18 | 1.37 | 15 |
| 5.1 | 43.96 | 5.3 | 4.96 | 0.63 | 15 |
| 3.0 | 27.67 | 3.5 | 1.66 | 0.16 | 15 |

DISCUSSION

Normal Decomposition

There is no marked variation in the composition of the products from 2–24% decomposition, implying that in this range of decomposition no secondary changes are occurring. Since the conversion in the present work is small, the ethane may be considered to be practically unchanged. The olefins, however, have a greater reactivity than the paraffins from which they are formed, and may undergo polymerization and hydrogenation as well as decomposition. The relative rates of the different types of secondary reactions are dependent on the initial concentrations of the individual decomposition products, the total pressure in the system, the temperature, etc. But at the conversions of the present work, this is not likely to be serious. Indeed, experiments carried out by Marek and McCluer (6) with $N_2-C_2H_4$ mixtures to determine the extent of ethylene decomposition under their experimental conditions showed the loss of C_2H_4 from this source to be slight. There is a further loss of unsaturateds by the reversal of the decomposition reaction. But pyrolyzing the butane to small extents as in the present work to eliminate secondary changes will also largely eliminate this difficulty. In any case, approximate calculations have shown that loss of products by reversible reaction is only likely to be of significance at pressures greater than atmospheric.

The slight variation in composition of the products with extent of decomposition establishes the validity of the extrapolation procedure for obtaining the initial products, the composition of which is found to be H_2 4.8%, CH_4 58.0%, C_2H_4 24.5%, and C_2H_6 12.0%. Steacie and Puddington (12) studied the decomposition of butane at 552°C. at conversions ranging from 12 to 50%. Assuming for purposes of comparison that H_2 , CH_4 , C_2H_4 , and C_2H_6 are their only products, the results of Steacie and Puddington, when recalculated on this basis, give the initial composition of the products as H_2 4.4%, CH_4 51.3%, C_2H_4 22.9%, and C_2H_6 21.3%. It is noteworthy that, whereas Steacie and

Puddington from 12 to 50% decomposition always found ethylene and ethane appearing in comparable quantities, in the present work the ratio of ethylene to ethane is approximately 2. This cannot be due to the difference in temperature of the two studies.

Within the temperature range of previous investigations (500–600°C.) it is usually stated that the products of the decomposition do not vary significantly with temperature. And such evidence as there is would seem to indicate that the relative probabilities of scission at the various bonds of a paraffin are only slightly affected by temperature. However, product paraffins higher than methane appear partly in the form of the corresponding olefins and hydrogen, and this effect while small at 440°C. might well be of significance at 600°C.

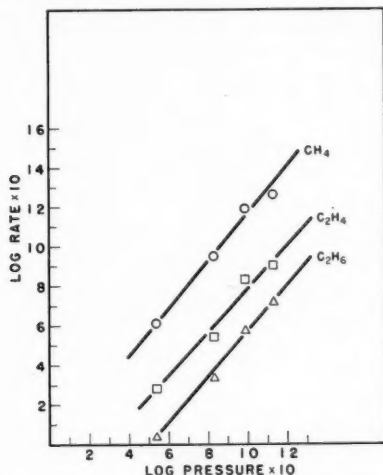


FIG. 5. Order determinations for the rates of formation of CH_4 , C_2H_4 , and C_2H_6 in the normal decomposition of butane.

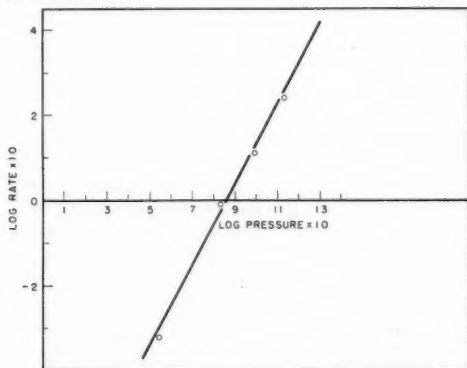


FIG. 6. Order determination for the rate of formation of hydrogen in the normal decomposition of butane.

So, on this basis, temperature might be anticipated to affect the olefin paraffin ratio in the products. The effect observed here, however, is opposite to that which might have been expected from this reasoning.

The rates of formation of all four products decrease markedly with decreasing butane pressure. From a plot of log rate vs. log pressure, Figs. 5 and 6, orders of 0.9, 1.1, 1.0, and 1.1 were obtained for the rates of formation of H_2 , CH_4 , C_2H_4 , and C_2H_6 respectively. Pease (7) investigated the decomposition of butane between 480 and 535°C. and from 10 to 60 cm. pressure. Comparison of times to 10% decomposition for different initial pressures indicated an order of 1.3, while if the initial portions of any curve were to be fitted, an order of as high as 5 or 6 was obtained.

Recently Stubbs and Hinshelwood (13) showed that for the normal decomposition, the variation of the initial rate (mm./min.) with initial pressure could be expressed by an empirical equation of the form

$$r_0 = Ap_0 + Bp_0^2$$

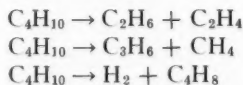
where $A/B = 2.45 \times 10^3$ for *n*-butane at 530°C.

An expression of this type does not correspond to any definite order for the slope of the log rate - log pressure plot would manifest a trend from the first order at low pressures to the second at infinite pressure. If, however, an expression such as the above applies not only to the over-all rate but also the rates of formation of the individual products, then at low pressures first order kinetics would be observed as found in the present work in the range 4-13 cm.

Fully Inhibited Reaction

Table II shows quite clearly that under the experimental conditions obtained in the present work, the composition of the products of the inhibited reaction is significantly different from that of the normal decomposition. In particular, the products of the inhibited decomposition contain proportionately more methane and less ethane than is found in the normal decomposition. This result is in striking contrast to all previous work which indicated that the composition of the products of the inhibited reaction was the same as that of the normal decomposition. Indeed, the identity of the composition of the products was regarded by Steacie and Folkins (11) as evidence for doubting the hypothesis

of complete suppression of chains, for it meant that in the case of butane for example the three separate molecular splits

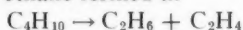


would have to occur in just the right ratio to give the same composition of products as occurred in the normal decomposition.

In previous work, samples for analyses were obtained at too great extents of decomposition. This is a distinct disadvantage for it has been shown (10) that in the later stages of the decomposition there is little or no difference

between the rate in the presence or absence of NO. This means that, as the butane decomposition progresses and the concentration of olefins increases, the inhibiting effect of the latter swamps that of the NO; as a result the rate of the NO-inhibited reaction approaches that of the normal rate in its later stages. In view of this, it is all the more surprising that the composition of the products of the inhibited reaction at large conversions should have been found to be the same as that of the normal decomposition.

Very recently Stubbs, Spall, Ingold, and Hinshelwood (14) found that at low pressures (8 mm.) the composition of the products of the inhibited reaction is indeed different from that of the normal, the former being proportionately richer in H_2 and C_2H_4 , and poorer in ethane than the latter. They concluded that the fate of the ethane formed in



is pressure dependent, the fraction of the primary ethane which undergoes decomposition into hydrogen and ethylene increasing as the pressure diminishes. If this is indeed so, it will explain why earlier investigators whose experiments were conducted at high pressures found the composition of the products of the inhibited and normal decompositions to be identical.

Comparison of the composition of the products obtained in the present work with that found by Stubbs *et al.* (4) is shown in Table IV.

TABLE IV
COMPARISON OF COMPOSITION OF THE PRODUCTS OBTAINED IN PRESENT WORK WITH THAT FOUND BY STUBBS *et al.*

| Products | Present work | | Stubbs <i>et al.</i> | |
|----------|-------------------------|---|-------------------------|--|
| | Normal decomposition, % | Fully inhibited decomposition sampled at 2% conversion, % | Normal decomposition, % | Fully inhibited decomposition sampled at 13% conversion, % |
| H_2 | 5 | 4.4 | 3.2 | 16.3 |
| CH_4 | 58 | 68.9 | 48.5 | 39.9 |
| C_2H_4 | 24 | 24.5 | 27.5 | 36.3 |
| C_2H_6 | 12 | 1.9 | 20.7 | 7.5 |

It is apparent that the only respect in which the present work agrees with that of Stubbs *et al.* is that the products of the inhibited reaction are poorer in ethane than the products of the normal decomposition. The genuineness of this result was recently confirmed by independent experiments carried out in collaboration with Dr. A. T. Blades in these laboratories. It should be noted, however, that there is no real reason why the two sets of results should be identical for they were obtained under different conditions. At small extents of decomposition, the manifestation of surface effects is more likely to be pronounced although this should have been reduced to a minimum in the present work in virtue of the large reaction vessel which was used.

The results of the present investigation have shown quite clearly that for the fully inhibited decomposition the rates of formation of the products are

variable. This substantiates the findings of Stubbs and Hinshelwood, who noticed that for the nitric oxide fully inhibited reaction there is often an induction period and that this determines the initial rate. Furthermore, for *n*-butane the rate of the normal decomposition is unaffected by an increase of surface whereas that of the fully inhibited decomposition was markedly reduced. It was therefore concluded that the uncontrolled variations appearing with butane are of the same nature as those caused by an increase of surface.

It is to be emphasized, however, that although this disturbance gives rise to variable rate measurements, the present work shows that the proportions in which the products are formed seems to be roughly invariable. For this reason it is felt that no very definite pronouncements can be made from a comparison of the composition of the products resulting from the normal and fully inhibited decompositions.

It has been shown (14) that the decomposition of a paraffin reduced to its limiting rate has an unusual pressure dependence. Thus, the order of this reaction is of the second at low pressures, then decreases to the first order, increases again to the second, and finally at the highest pressures employed became first order once again.

The data given in Table III, when plotted in the conventional manner (Fig. 7) gave orders of 2.4 and 3.0 respectively for the rates of formation of C_2H_4 and C_2H_6 . No significance is attached to these values for order only has

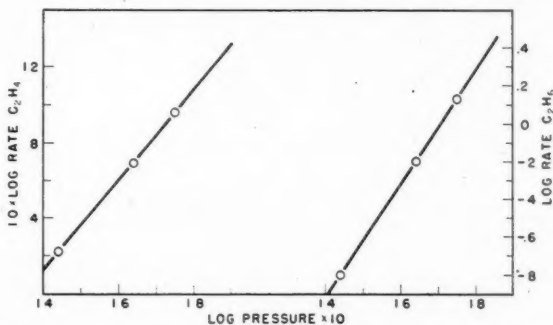
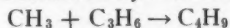


FIG. 7. Determination of "order" for the rates of formation of C_2H_4 and C_2H_6 in the nitric oxide inhibited decomposition of butane.

meaning when the dependence of the rate on pressure is restricted to a function of the form $\text{rate} \propto p^n$. However, since the rates here were determined analytically, whereas those of Stubbs *et al.* refer to the over-all rates determined from pressure increases, the present result confirms that the dependence of the rate on pressure is complex.

The efficiencies of propylene and nitric oxide were recently compared (13) in the inhibition of *n*-pentane, when it was found that C_3H_6 is about 1/12 as efficient as nitric oxide. When propylene is used as an inhibitor, it is highly unlikely that radicals will be removed by the reaction



for at the temperature of the experiment (530°C.) breakdown of C_4H_9 would be almost complete and radicals would therefore be regenerated. It seems more reasonable to assume the reaction



The resulting allyl radical is known to be stable and will dimerize to form diallyl rather than continue the chain. On this basis it is possible to use information which is now available to compute the relative rates at 530°C. of the following two reactions



With $E_1 = 7.7$ kcal. and $P_1 = 9 \times 10^{-4}$ (15) $k_1 = 7 \times 10^{-7}Z$, where Z is the collision number.

For reaction [2] a collision yield of 1.5×10^{-4} at room temperature was obtained (2). This may mean either $E_2 = 5.7$ kcal. and $P_2 = 1$ or $E_2 = 0$ and $P_2 = 1.5 \times 10^{-4}$ or some intermediate values. Considering the two extreme cases and assuming the collision numbers to be approximately the same

$$\begin{aligned} \frac{\text{Rate of 2}}{\text{Rate of 1}} \text{ at } 530^\circ\text{C.} &= \frac{5 \times 10^{-2}}{7 \times 10^{-7}} \text{ or } \frac{1.5 \times 10^{-4}}{7 \times 10^{-7}} \\ &= 10^5 \text{ or } 2 \times 10^2. \end{aligned}$$

The great discrepancy between the computed and observed relative rates may mean either that the mechanism of inhibition is incorrect or, if it is correct, that NO is very much less efficient as an inhibitor than might have been expected. A reason has already been given for regarding the association reaction $CH_3 + C_3H_6 \rightarrow C_4H_9$ as highly improbable at 530°C. The problem is therefore to explain the relative inefficiency of nitric oxide as an inhibitor compared with propylene. Lack of definite information, however, prevents further discussion of the problem at this stage.

ACKNOWLEDGMENTS

Grateful acknowledgment is made to Dr. F. P. Lossing and Miss F. Gauthier for numerous mass spectrometric analyses. We are also indebted to Mr. R. Pilon for perfecting the technique for ensuring that the C_2 fractions were free from nitric oxide.

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A CHEMICAL SYNTHESIS OF OCTA-O-ACETYL- β -D-MALTOSE¹

By R. U. LEMIEUX

ABSTRACT

Reaction of tri-*O*-acetyl-D-glucosan (1, 5) α (1, 2) with 1,2,3,6-tetra-*O*-acetyl- β -D-glucose at 120°C. for 13 hr. followed by acetylation and then chromatographic separation of the products afforded octa-*O*-acetyl- β -D-maltose in about 8% yield.

Brigl (2) found that tri-*O*-acetyl-D-glucosan (1, 5) α (1, 2) reacts readily with methanol to form methyl 3,4,6-tri-*O*-acetyl- β -D-glucopyranoside in almost quantitative yield. Hickinbottom (8) and Hardegger and de Pascual (5) have applied the method for the preparation of a variety of alkyl- β -D-glucopyranosides. In 1943, Montgomery, Richtmyer, and Hudson (12) interpreted the reaction of Brigl's anhydride with methanol as proof for the configuration of the anomeric center in methyl- β -D-glucopyranoside.

Although the Brigl anhydride yields β -D-glucopyranosides on reaction with alcohols at ordinary temperatures, evidence has long existed which indicates that α -D-glucopyranosides tend to be formed at elevated temperatures. In 1928, Hickinbottom (8) reported the preparation of phenyl- α -D-glucopyranoside by reaction of the anhydride with phenol at 100°C. for 20 hr. In 1931, Haworth and Hickinbottom (6) reacted the anhydride with 2,3,4,6-tetra-*O*-acetyl- β -D-glucose in benzene at 90°–100°C. for 37 hr. to form a hepta-*O*-acetyl derivative of a nonreducing disaccharide termed *neotrehalose* which appeared to be α -D-glucopyranosyl- β -D-glucopyranoside. In this case, the origin of the α -D-linkage could not be decided upon since it was possible that under the reaction conditions used the 2,3,4,6-tetra-*O*-acetyl- β -D-glucose underwent anomericization before reaction with the anhydride. More recently, Hardegger and de Pascual (5) have reacted the anhydride with cholestanol at 120°C. for 16 hr. to form the α -D-glucopyranoside.

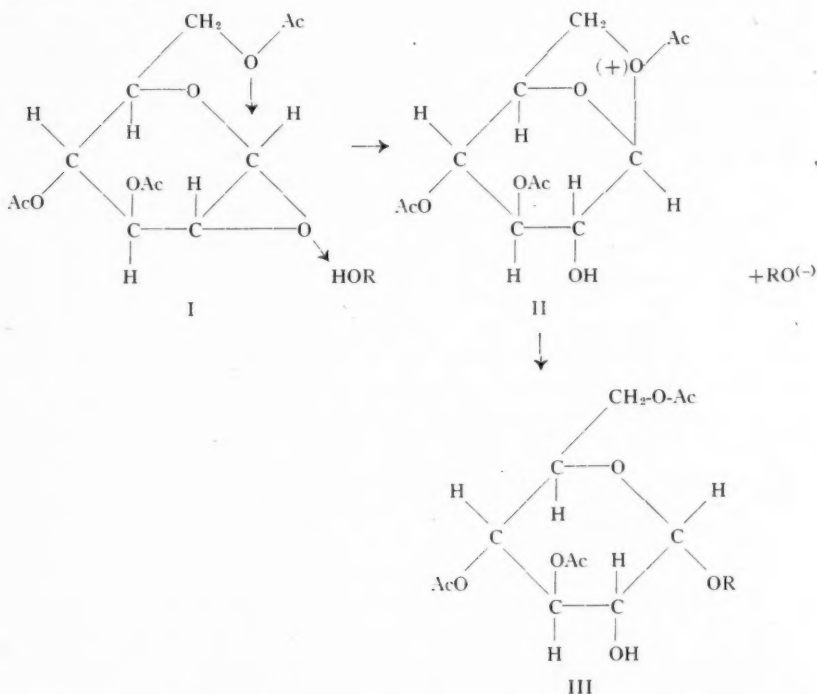
The discovery first made by Bardolph and Coleman (1) that alkaline hydrolysis of Brigl's anhydride yields D-glucosan (1, 5) β (1, 6) (3, 10), and the observation (10) that dissociation of the C1 to acetoxy group bond of 1,2,3,4-tetra-*O*-acetyl- β -D-glucopyranose with stannic chloride in chloroform yields tri-*O*-acetyl-D-glucosan (1,5) β (1,6), suggested to us (10) that the C6-oxygen atom of an α -D-glucopyranose derivative is capable of participation in replacement reactions at the anomeric center. Since direct replacements with retention of configuration are not known, the formation of α -glucosides from Brigl's anhydride requires the formation of an unstable intermediate from the anhydride. In the light of the above evidence for the ability of C6-substituents in glucose to participate in replacements at the lactol carbon atom, it seems probable that, at elevated temperatures and in the presence of an alcohol, the

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anhydride (I) is converted to the 1,6- β -D-cyclic ion (II) which is capable of interaction to yield an α -D-glucopyranoside (III).

Treatment of Brigl's anhydride with an equivalent amount of 1,2,3,6-tetra-*O*-acetyl- β -D-glucopyranose (7) at 120°C. for 13 hr. and acetylation of the product gave a sirup from which pure octa-*O*-acetyl- β -D-maltose was readily isolated in about 8% yield. The elegant procedure for the chromatographic separation of sugar acetates established by McNeely, Binkley, and Wolfrom (11) was used for the isolation. The substance was identified by mixed melting point determination and by comparison of its infrared absorption spectrum with that of a sample of octa-*O*-acetyl- β -D-maltose prepared by acetylation of maltose (9).



Although Pictet and Vogel (13) have reported the synthesis of maltose by heating β -glucose and α -glucose at 160°C. in a vacuum and by heating β -glucose and β -glucosan at 150°C. in vacuum with or without zinc chloride, Evans, Reynolds, and Talley (4, p. 35) have recently made the statement, "Of the common sugars, only those containing the sucrose and maltose type linkages still challenge the carbohydrate chemist to obtain them by a true chemical synthesis". Since octa-*O*-acetyl- β -D-maltose can be deacetylated readily to yield maltose (14), the present sequence of reactions make possible a true chemical synthesis of maltose.

EXPERIMENTAL

Octa-O-acetyl-β-D-maltose

Pure tri-*O*-acetyl-D-glucosan (1,5) α (1,2) (2), m.p. 58–59°C., 55 mgm., and 1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranose (7), m.p. 131–132°C., 60 mgm., were mixed in a tube and kept in a high vacuum at room temperature for 30 min. and then at 100°C. for 5 min. The tube was sealed and heated in an oil bath controlled at 120°C. for 13 hr. The hard, brown-colored reaction product was dissolved in 5 ml. of acetic anhydride and 100 mgm. of sodium acetate was added. After heating on the steam bath for one hour, the mixture was evaporated *in vacuo* to a salt cake. The residue was extracted with benzene to yield, on evaporation, a brown sirup.

The sirup was dissolved in about 2 ml. of benzene and added to the top of a 160 × 35 mm. column of a mixture, 50 gm., of five parts Magnesol and one part Celite (11) wetted with benzene. The chromatogram was developed with one liter of 250:1 benzene to ethanol mixture and the column extruded and streaked with a freshly prepared aqueous solution of 1% potassium permanganate in 2.5 *N* sodium hydroxide. Four distinct zones were observed and these were cut out and eluted with warm acetone. The first zone, 0–8 mm. from the top of the column, gave a dark brown sirup which was not investigated. The material from the second zone, 12–25 mm. from the top of the column, was crystallized from ethanol to yield 10.2 mgm. of a substance, m.p. 159–161°C., $[\alpha]_D^{20} +63^\circ$ (*c*, 0.36 in chloroform) which did not depress the melting point of an authentic sample of octa-*O*-acetyl-β-D-maltose, m.p. 161–162°C. The infrared spectrum of the substance, mulled with Nujol and measured with a Perkin-Elmer Model 21 double beam spectrometer, was identical with the spectrum obtained under the same conditions of the authentic sample of octa-*O*-acetyl-β-D-maltose. The third zone, 70–88 mm. from the top of the column, gave 2.4 mgm. of crystalline penta-*O*-acetyl-α-D-glucopyranose, m.p. 109–111°C. and the fourth zone, 110–128 mm. from the top of the column, gave 39.1 mgm. of penta-*O*-acetyl-β-D-glucopyranose, m.p. 131–132°C.

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The starting materials used in this work were prepared by Dr. H. F. Bauer and Dr. G. Huber.

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α -OBSCURINE AND β -OBSCURINE: STRUCTURE STUDIES¹

BY BARRY P. MOORE² AND LÉO MARION

ABSTRACT

The alkaloid hitherto described as obscurine has been shown to consist of a mixture of two bases, α -obscurine ($C_{17}H_{26}ON_2$) and β -obscurine ($C_{17}H_{24}ON_2$). Dehydrogenation of α -obscurine by heating with palladium-charcoal gives rise to 7-methylquinoline and 6-methyl- α -pyridone. The infrared absorption spectrum of the base shows absorption bands indicative of a carbonyl and of a secondary amino group, possibly in a cyclic lactam, while absorption in the ultraviolet indicates the presence of a double bond conjugated with the carbonyl group. β -Obscurine on the other hand contains an α -pyridone ring as shown by its infrared absorption spectrum and also by the similarity of its ultraviolet absorption spectrum with that of 6-methyl- α -pyridone.

Obscurine (alkaloid L6) was first reported as occurring in *Lycopodium flabelliforme* L. (2) and later in *L. annotinum* L. (3) although it had first been isolated from *L. obscurum* L. var. *dendroideum* (Michx.) D. C. Eaton (4). It was described as a crystalline base melting at 282°, yielding analytical figures corresponding to the empirical formula $C_{18}H_{28}ON_2$, and forming a crystalline diperchlorate hydrate melting at 299°. On reanalysis of the base it was found difficult to obtain consistent results and an attempt was made to purify the base further. Repeated recrystallization of the base failed to effect a separation, but by chromatography on alumina it was possible to separate it into a main fraction and a small quantity of a second base. The main fraction which will be designated α -obscurine melted at 283–284° (dec.) and formed a monopicrate, m.p. 133–134°. The second base, which it is proposed to name β -obscurine, melted at 322–323° (dec.) and formed a monopicrate, m.p. 254°. From numerous analyses of the bases and their picrates it appeared that the most probable formulae were $C_{17}H_{26}ON_2$ for α -obscurine and $C_{17}H_{24}ON_2$ for β -obscurine. The perchlorates were prepared but they both absorbed water very readily and were not analyzed.

The infrared absorption spectrum of α -obscurine in chloroform solution showed a small absorption peak at 3411 cm^{-1} indicative of a secondary amino group and a broad band at 1667 cm^{-1} attributable to a carbonyl group. The infrared spectrum of β -obscurine contained an absorption peak indicative of a secondary amino group at 3385 cm^{-1} , and a strong double peak at 1659 cm^{-1} , 1651 cm^{-1} with smaller peaks at 1620 cm^{-1} and 1613 cm^{-1} suggestive of an α -pyridone (5) (Fig. 1).

On dehydrogenation by heating with palladium-charcoal, α -obscurine gave rise to 7-methylquinoline and to 6-methyl- α -pyridone, both identified by comparison with synthetic specimens. The infrared absorption spectrum of 6-methyl- α -pyridone in chloroform solution (Fig. 1) showed a small peak at 3387 cm^{-1} due to the imino group, a band at 1662 cm^{-1} (77%), and one at

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² National Research Council of Canada Postdoctorate Fellow, 1950–1951.

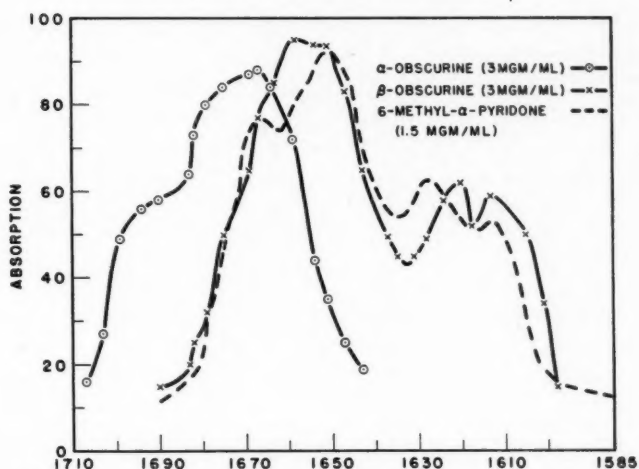


FIG. 1. Infrared spectra of chloroform solutions of α -obscurine, β -obscurine, and 6-methyl- α -pyridone, measured on Perkin-Elmer 12B single beam spectrometer with a calcium fluoride prism.

1651 cm^{-1} (92%) together with smaller peaks at 1628 cm^{-1} and 1613 cm^{-1} attributable to the α -pyridone structure. The similarity in position between these absorption bands and those appearing in the same region in the infrared spectrum of β -obscurine indicate that an α -pyridone ring must be present in β -obscurine. The infrared spectrum of α -obscurine shows that in that alkaloid the nitrogen is possibly part of a cyclic lactam which, however, is not a pyridone. In the infrared spectrum of a substituted dihydro- α -pyridone, the carbonyl band would be expected to occur either at the same place or at a lower wave number than it does in the spectrum of β -obscurine (5). In the spectrum of octahydrogelsemine, which contains a saturated five-membered lactam, the carbonyl band is observed at about 1690 cm^{-1} . It is therefore possible that the α -pyridone obtained by the degradation of α -obscurine is an artefact obtained by ring enlargement of a five-membered cyclic lactam. A comparison of the ultraviolet absorption spectra (Fig. 2) of β -obscurine (max. λ 232 $\text{m}\mu$, $\log \epsilon$, 3.98; λ 315 $\text{m}\mu$, $\log \epsilon$, 3.89) and 6-methyl- α -pyridone (max. λ 229 $\text{m}\mu$, $\log \epsilon$, 3.87; 304 $\text{m}\mu$, $\log \epsilon$, 3.83) shows that they are almost identical and supports the conclusion drawn from the infrared evidence. On the other hand, the ultraviolet absorption spectrum of α -obscurine (Fig. 2) (max. λ 255 $\text{m}\mu$, $\log \epsilon$, 3.75) differs markedly and seems to indicate the presence of a cyclic lactam containing $\alpha\beta$ -unsaturation. $\alpha\beta$ -Unsaturated seven-membered cyclic lactams show a maximum at about 240 $\text{m}\mu$ in the ultraviolet (1,6). It has not been possible, however, to find in the literature ultraviolet absorption curves of $\alpha\beta$ -unsaturated five- or six-membered cyclic lactams. Nevertheless, it has to be added that α -obscurine and β -obscurine are very similar not only in their empirical formulae but in their properties. 6-Methyl- α -pyridone and both α -obscurine and β -obscurine produce an orange-red color with aqueous

ferric chloride and they couple with diazotized sulphanilic acid to produce a deep orange-red product.

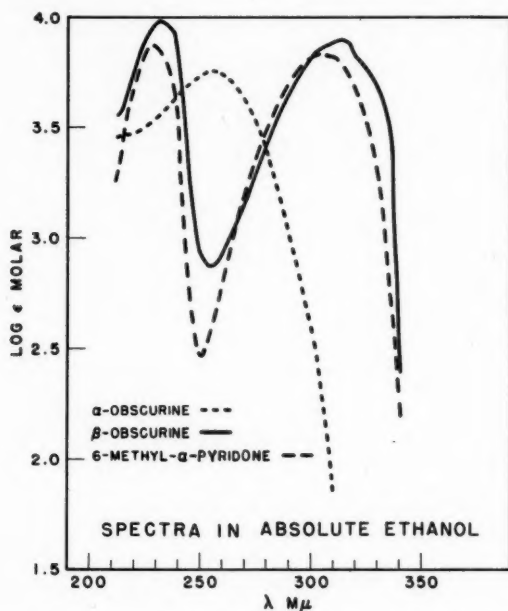


FIG. 2. Ultraviolet absorption spectra taken in absolute ethanol with a Beckman quartz spectrophotometer.

An attempt to dehydrogenate α -obscurine to β -obscurine by bromination followed by dehydrobromination altered the compound but did not give β -obscurine.

Both fragments obtained in the degradation of α -obscurine together provide 16 carbon atoms and therefore one carbon only is missing to complete the skeleton of the alkaloid. The empirical formulae of the bases require in each case a structure containing four rings. Since the degradation products account for three rings it may be assumed that the missing carbon is in a methylene group forming part of the fourth ring.

EXPERIMENTAL³

Purification of Obscurine

Obscurine, recrystallized twice from chloroform-methanol, consisted of colorless prisms, m.p. 281–282°. A quantity of recrystallized obscurine (500 mgm.) dissolved in a mixture of chloroform (25 ml.) and petroleum ether (75 ml. b.p. 30–60°) was chromatographed on alumina and eluted first with 1:1 chloroform-petroleum ether (140 ml.), 3:1 chloroform-petroleum ether (60 ml.), chloroform (30 ml.), 1:1 methanol-chloroform (40 ml.), and finally with

³ All melting points are corrected.

pure methanol. Two fractions, A (408 mgm.) and B (92 mgm.) were thus obtained from the chromatogram. Fraction A was practically all present in the 1:1 chloroform-petroleum ether eluate, while fraction B was all obtained from the 1:1 methanol-chloroform eluate.

α -Obscurine

Fraction A, which was crystalline, was recrystallized twice from methanol from which it separated as colorless prisms, m.p. 283–284°. Rechromatography of a sample of this base (now designated α -obscurine) showed that it was homogeneous. Calc. for $C_{17}H_{26}ON_2$: C, 74.41; H, 9.55; N, 10.21. Found: C, 74.80, 74.17; H, 9.80, 9.12; N, 10.45%. No imino-methyl group was present. A quantity of α -obscurine was dissolved in chloroform and to it was added an ethereal solution of picric acid. The picrate crystallized out and after recrystallization from methanol-ether it consisted of yellow needles, m.p. 135°. Drying at 100° at 0.1 mm., over phosphoric anhydride did not alter the melting point. Calc. for $C_{17}H_{26}ON_2 \cdot C_6H_3O_7N_3$: C, 54.86; H, 5.81; N, 13.91. Found: C, 54.39, 54.45; H, 6.10, 6.14; N, 14.19, 14.39%. In contact with aqueous ferric chloride it produced an orange-red coloration. On coupling with diazotized sulphanilic acid α -obscurine produced a deep orange-red color.

A small quantity of α -obscurine was dissolved in methanol, the solution neutralized with perchloric acid and diluted with ether. The precipitated perchlorate was recrystallized from ethyl acetate containing a drop of perchloric acid. It separated as colorless prisms, m.p. 255° (dec.), but was too soluble and deliquescent to constitute a characteristic derivative and was not analyzed.

β -Obscurine

Fraction B of the chromatogram was crystalline and after recrystallization from methanol consisted of colorless prismatic rods, m.p. 322–323° when immersed at 240°. Calc. for $C_{17}H_{24}ON_2$: C, 74.96; H, 8.88; N, 10.29. Found: C, 75.18, 74.67; H, 8.62, 8.47; N, 10.22%. The imino-methyl determination was negative. β -Obscurine with aqueous ferric chloride produced an orange-red color and on coupling with diazotized sulphanilic acid gave a lighter orange-red color. An ethereal solution of picric acid was added to a small quantity of this base (now designated β -obscurine) in chloroform. The crystalline precipitate was recrystallized twice from methanol from which it separated as yellow plates, m.p. 254° (dec.). Calc. for $C_{17}H_{24}ON_2 \cdot C_6H_3O_7N_3$: C, 55.08; H, 5.43; N, 13.97. Found: C, 54.89, 54.90; H, 5.60, 5.06; N, 13.85%.

The perchlorate prepared from β -obscurine in the usual way consisted of colorless needles, m.p. 322° (dec., with previous darkening). Like the perchlorate of α -obscurine it was very soluble in methanol and in water and was not analyzed.

Dehydrogenation of α -Obscurine

α -Obscurine (200 mgm.) and freshly prepared palladium-charcoal (50 mgm., 5% Pd) were thoroughly mixed and heated in a small bulb in a Wood's metal bath to 290° under a slow stream of dry oxygen-free nitrogen. The exit gas was washed in a trap containing *N*/1 aqueous hydrochloric acid. Sublimation of

the α -obscurine occurred at first but when decomposition had started the refluxing product washed the crystals down again. After 30 min. the temperature of the bath was lowered to 280° and maintained at this temperature for 90 min. After cooling, the reaction mixture was extracted with chloroform and the extract filtered and evaporated to remove the solvent. There was left an oily residue which when distilled *in vacuo* yielded the following fractions: (I) colorless liquid, b.p. 95–105° at 0.5 mm., wt. 20 mgm. (II) a solid subliming at 115–125° at 0.5 mm., wt. 12 mgm. (III) a resin, b.p. 190–220° at 0.5 mm., wt. 20 mgm.

7-Methylquinoline

Fraction I (20 mgm.) was dissolved in ether and to the solution an ethereal solution of picric acid was added as long as a precipitate formed. The liquid was decanted and the precipitate washed with ether and dissolved in boiling methanol. The solution was evaporated down to a volume of 5 ml. which on cooling deposited a small quantity of yellow needles. After recrystallization from methanol the picrate melted at 235°. In admixture with an authentic specimen of 7-methylquinoline picrate (m.p. 241°) it melted at 238°. A small quantity of picrate was also obtained from fraction II.

6-Methyl- α -pyridone

Fraction II (12 mgm.) consisted of crystals contaminated with a small quantity of an oily base which was removed by washing with petroleum ether. This base was converted to a picrate which proved identical with 7-methylquinoline picrate. The solid which had been washed with petroleum ether was crystallized from acetone – petroleum ether from which it separated as cream-colored prisms. This crystalline product was sublimed at 115–120° at 0.1 mm. and the sublimate consisted of clusters of colorless prisms, m.p. 158.5°. Calc. for C_6H_7ON : C, 66.03; H, 6.47; N, 12.84. Found: C, 67.66; H, 7.23; N, 12.60%. The analysis, which is not too satisfactory, was performed on extremely small quantities and could not be repeated. The compound, however, gave an orange-red color with aqueous ferric chloride and a deep orange-red product on coupling with diazotized sulphanilic acid. The infrared absorption spectrum of the substance (Fig. 1) showed an absorption band at 3387 cm^{-1} indicative of an NH group, a double carbonyl band at 1662–1651 cm^{-1} , and smaller bands at 1628 and 1613 cm^{-1} usually attributable to a pyridone structure. It was assumed that the compound was 6-methyl- α -pyridone and this substance was synthesized as described by Simonsen (7) by the diazotization of 2-amino-6-methylpyridine. The synthetic substance consisted of cream-colored prisms, m.p. 158–159°, and admixture with the degradation compound failed to depress the melting point. Both substances gave similar color tests with aqueous ferric chloride and reacted in an identical manner with diazotized sulphanilic acid. Synthetic 6-methyl- α -pyridone was sublimed *in vacuo* for use in the determination of the ultraviolet and infrared absorption spectra. Both these spectra were respectively superimposable on the corresponding spectra of the degradation product.

ACKNOWLEDGMENT

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THREE MINOR ALKALOIDS OF *GELSEMIUM SEMPERVIRENS* AIT.¹

BY H. SCHWARZ² AND LÉO MARION

ABSTRACT

After the removal of gelsemine and sempervirine from the extract of the root of *Gelsemium sempervirens* Ait. the residual alkaloids left in the mother liquors were benzoylated. It was thus possible to separate the tertiary bases from the secondary bases which were obtained as a mixture of the neutral benzoyl derivatives. Purification by chromatography yielded the benzoylated mixture in crystalline form. This was hydrolyzed and the recovered secondary bases were separated by fractional crystallization of the perchlorates into alkaloid A and alkaloid B. Alkaloid A was shown by direct comparison to be identical with the gelsemicine ($C_{20}H_{28}O_4N_2$) of Chou. Alkaloid B, now designated gelsedine, was shown to be distinct from either gelsemicine or gelsemine. It appears to be identical with the alkaloid $C_{19}H_{25}O_3N_2$ claimed by Janot and his co-workers to be gelsemicine. From the tertiary bases there was isolated an apparently new base, gelseverine, as its crystalline perchlorate. Whereas gelsemine is a 3,3-disubstituted oxindole, gelsedine appears to be a 1,3-disubstituted oxindole and gelseverine a 1,3,3-trisubstituted oxindole. Gelsemicine shows many of the characteristics of an indole alkaloid.

Besides the two previously known alkaloids, gelsemine and sempervirine, Chou (3) isolated from the root of *Gelsemium sempervirens* Ait. a third base, gelsemicine, m.p. 171°, $[\alpha]_D -140^\circ$ to which he assigned the empirical formula $C_{20}H_{28}O_4N_2$ [sic]. Chou (3) also described the hydrochloride of the base, m.p. 140°.

From the same plant Forsyth, Marrian, and Stevens (4) also isolated gelsemicine. They reported m.p. 170°, $[\alpha]_D -140^\circ$, but corrected the formula to $C_{20}H_{24-26}O_4N_2$. According to those authors gelsemicine forms a picrate, m.p. 203°, yields a nonbasic monobenzoyl derivative, m.p. 232°, and behaves as a secondary base giving rise when treated with methyl iodide to N-methyl-gelsemicine hydriodide, m.p. 227°. It is inert towards the usual carbonyl reagents (4). Raymond-Hamet (7) compared the ultraviolet absorption spectrum of Chou's gelsemicine with the spectra of other alkaloids and concluded that gelsemicine contained an indole nucleus.

More recently, Janot, Goutarel, and Friedrich (5) isolated and described a base that they assumed to be the alkaloid gelsemicine although they reported m.p. 171°, $[\alpha]_D -160^\circ$, and they proposed the quite different empirical formula $C_{19}H_{24}O_3N_2$. They prepared the benzoyl derivative, m.p. 262°, $[\alpha]_D -117^\circ$, and the N-methyl base, m.p. 134°. According to them the basic nitrogen of their base is secondary and the base contains two active hydrogens. Furthermore, its ultraviolet absorption spectrum resembles that of gelsemine (oxindole). Their publication, however, contained no experimental section.

In the course of our work on gelsemine the isolation of the alkaloids of *G. sempervirens* has been reinvestigated as already reported in a preliminary

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note (9). By modifying the usual procedure (see experimental part) it was possible to increase the yield of gelsemine from 36 gm. to 58 gm., and the yield of sempervirine nitrate from 18 gm. to 42 gm. per 22.6 kgm. of dry ground root. The modification consisted in adsorbing on filtercel the tarry residue obtained after evaporation of the methanol percolate of the plant material. This supplies a large adsorption surface and can as in this case overcome the difficulties always arising in the process of working up plant extracts containing a large amount of water-insoluble tarry material. It has the advantage of not leaving the alkaloids in long contact with alkali, thus avoiding the loss of alkali-sensitive natural products. The method can be recommended especially for quaternary bases of which mostly all salts are only slightly soluble in water, e.g. sempervirine, serpentine, alstonine, berberine, etc. Gelsemine and sempervirine together constituted about 75% of the alkaloid content of the root while the remaining 25% was to be found in the mother liquors. The accumulation of relatively large quantities of alkaloid-rich mother liquors prompted us to attempt the isolation of the minor alkaloids present in the plant.

The basic residue obtained by evaporation of the mother liquors was separated into secondary and tertiary bases by benzylation or acetylation. Benzylation yielded a basic fraction containing the tertiary bases and a neutral fraction which represented the secondary bases. The latter was purified by chromatography and produced a crystalline benzoylated product, the melting point of which (233–240°) was not improved by recrystallization. A chromatogram of the crystalline substance furnished fractions differing in melting points, but infrared absorption spectra showed that none of these fractions consisted of a pure compound. This method of direct separation of the benzoylated bases was abandoned because the middle fractions were too large and the separation proved too laborious and unsatisfactory.

The benzoylated product was hydrolyzed and the free base crystallized from ethyl acetate. It melted at 136–139°, which was 32–35° lower than the reported melting point of gelsemicine and had $[\alpha]_D -150^\circ$, a value intermediate between the two figures previously reported (3, 4, 5). Fractional crystallization did not yield any higher melting crop, although some fractions contained two distinct forms of crystals, i.e., large stout rhombs and elongated rhombs. The alkaloids could not be chromatographed as they decomposed on the column.

Acetylation instead of benzylation was not conducive to better results. Chromatography and fractional crystallization of the acetylated product both led in small yield to a fraction, m.p. 161°. On hydrolysis this fraction gave a base, m.p. 162–165°, which could not be purified further by recrystallization.

The crystalline base obtained by hydrolysis of the benzoylated product formed a picrate which could be separated into two fractions, each of which, however, still consisted of a mixture.

Finally, a successful method of separation was found in the fractional crystallization of the perchlorates. In the course of an attempt to prepare a perchlorate from the free base (obtained by hydrolysis of the crystalline benzoylated product), it was noted that the yield of crystalline salt was at best

75%, and that on further recrystallization the yield decreased to about 40–50%. This perchlorate was almost insoluble in the cold solvent (methanol-water 1:1); it melted at 183° and yielded analytical figures in agreement with the formula $C_{19}H_{24}O_3N_2 \cdot HClO_4$. From the final mother liquors no more perchlorate could be induced to crystallize thus suggesting that separation had

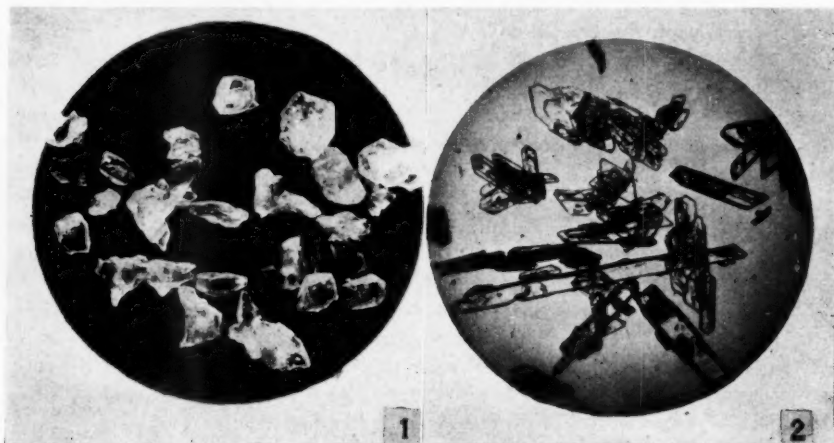


FIG. 1. Photomicrograph of gelsemicine crystals. $\times 5$

FIG. 2. Photomicrograph of gelsedine crystals. $\times 20$

been effected into a sparingly soluble crystalline perchlorate and a very soluble perchlorate. The latter when decomposed yielded alkaloid A while decomposition of the crystalline perchlorate gave alkaloid B. Both bases were obtained as prismatic crystals, but these were readily distinguishable as shown in Figs. 1 and 2.

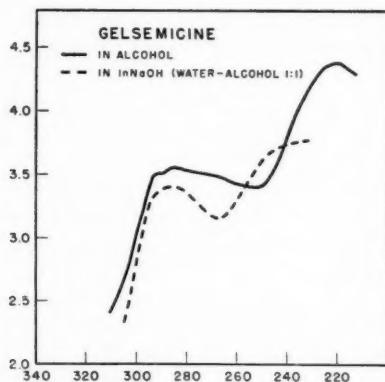


FIG. 3. Ultraviolet spectra of gelsemicine.

Alkaloid A, m.p. 171–172°, $[\alpha]_D -142^\circ$, yielded analytical figures corresponding to the empirical formula $C_{20}H_{26}O_4N_2$. It formed a picrate, m.p. 206–208°,

a benzoyl derivative, m.p. 235–236°, $[\alpha]_D -106^\circ$, and an acetyl derivative, m.p. 174–175°. Alkaloid B, m.p. 172.5–174°, $[\alpha]_D -158^\circ$, gave analytical figures corresponding to the formula $C_{19}H_{24}O_3N_2$. It formed a picrate, m.p. 224–226°, a benzoyl derivative, m.p. 251–252°, and an acetyl derivative, m.p. 165–166°. Alkaloid A was quite distinct from alkaloid B, but it had the

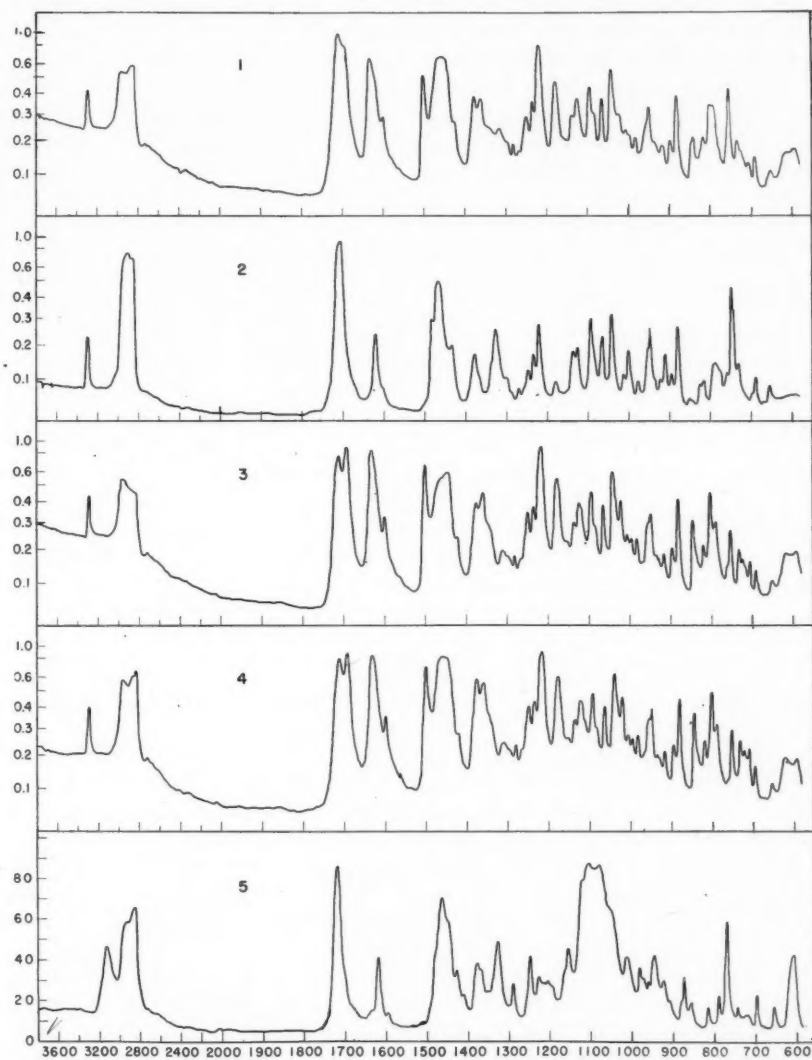


FIG. 4. Infrared absorption spectra in Nujol mull. curve 1, mixture of gelsemicine and gelsedine; curve 2, gelsedine; curve 3, gelsemicine; curve 4, Chou's gelsemicine; curve 5, gelsevirine perchlorate.

same physical constants and so had its picrate and benzoyl derivative as those reported by Chou (3) for gelsemicine and by Forsyth, Marrian, and Stevens (4) for the corresponding derivatives. Both the ultraviolet (Fig. 3) and the infrared absorption spectra of alkaloid A were superimposable on the corresponding spectra of a sample of Chou's gelsemicine which was kindly supplied to us by Dr. Raymond-Hamet (curves 3 and 4, Fig. 4). Furthermore, alkaloid A showed no depression in melting point in admixture with Chou's alkaloid. It is therefore identical with gelsemicine.

The physical constants of alkaloid B and its derivatives (except for the melting point of its benzoyl derivative) were very close to those described by Janot, Goutarel, and Friedrich (5) for the alkaloid, which they assumed to be gelsemicine, and its derivatives. The empirical formulae of the bases were identical and so was the maximum in their ultraviolet absorption spectra (Fig. 5). It seems, therefore, highly probable that alkaloid B is identical with

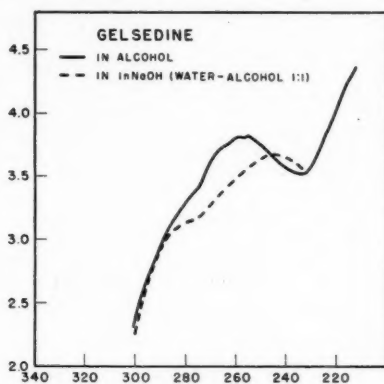


FIG. 5. Ultraviolet spectra of gelsedine.

Janot's "gelsemicine" and since it is quite different from Chou's gelsemicine, it is proposed to designate this new base as gelsedine.

Alkaloid A (gelsemicine) and alkaloid B (gelsedine) on admixture showed a melting point depression, the melting point of the mixture ($136-139^{\circ}$) being the same as that observed for the original mixture before separation. The acetyl derivatives also showed a melting point depression on admixture. The mixed picrates melted in a range between the melting points of the pure picrates, but a definite depression could be observed after prolonged grinding of the mixture in a mortar. The benzoyl derivatives, however, did not show a melting point depression under any condition.

From the basic fraction separated from the benzoylation reaction mixture, alkaloid C was isolated as the perchlorate, m.p. $251-252^{\circ}$. The liberated base was a noncrystallizable oil and it formed an oily picrate. It, however, furnished a crystalline methiodide, m.p. $259-262^{\circ}$ (dec.). The analytical figures of the perchlorate indicated for the base the empirical formula $C_{21}H_{24}O_3N_2$, although those obtained from the distilled base and from the methiodide agreed better

with $C_{21}H_{26}O_3N_2$. The infrared absorption spectrum of the perchlorate (curve 5, Fig. 4) showed that alkaloid C was not identical with any so far identified from *G. sempervirens* and was therefore probably new. It is proposed to designate this alkaloid as gelsevirine. Forsyth, Marrian, and Stevens (4) reported the isolation of a methiodide, m.p. 261° , but the analytical figures of this salt did not agree with those found for gelsevirine.

The mother liquor from which gelsevirine perchlorate separated contained more alkaloidal material, but it has not yet been possible to identify any further bases (see experimental).

Gelsedine ($C_{19}H_{24}O_3N_2$) contained one methoxyl, one imino-methyl, one C-methyl, and one active hydrogen (Janot and his co-workers (5) report two active hydrogens for their base). Its infrared absorption spectrum (curve 2, Fig. 4) showed an NH band, a carbonyl band, and a band (1620 cm^{-1}) characteristic of a benzene ring. The ultraviolet spectrum (Fig. 5) in alcohol showed a minimum at $235\text{ m}\mu$, a maximum at $258\text{ m}\mu$, and a shoulder at $280\text{ m}\mu$. In acidic solution the absorption was about the same. In aqueous alkali gelsedine dissolved slowly with the development of a bright yellow color. In aqueous-alcoholic alkali, however, the color did not develop immediately and in such a solution the absorption in the ultraviolet was shifted giving a maximum at $244\text{ m}\mu$ and a shoulder at $280\text{ m}\mu$. However, if the spectrum of this solution was measured after some lapse of time, the maximum was shifted below $230\text{ m}\mu$, the shoulder became a maximum and a new absorption band developed in the visible ($405\text{ m}\mu$). It is noteworthy that this spectrum is very similar to that of N-methyl-isatin.

Both acetyl and benzoyl gelsedine were neutral substances no longer containing active hydrogen. Acetyl gelsedine, which, as expected, contained two C-methyl groups, had the same ultraviolet absorption as gelsedine in alcohol. The infrared absorption spectrum of benzoylgelsedine in nujol mull or in chloroform solution (Fig. 6) showed no absorption in the NH, OH region, and contained the two expected bands in the carbonyl region.

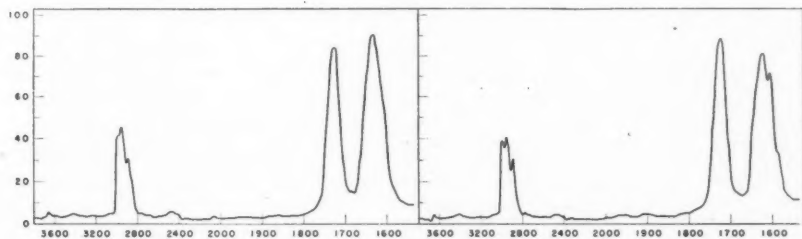


FIG. 6. Infrared spectra in chloroform solution. Left, acetyl-gelsedine. Right, benzoyl-gelsedine.

In glacial acetic acid solution over Adams' catalyst at room temperature gelsedine was not hydrogenated but at $60\text{--}70^\circ$ it took up hydrogen very slowly giving rise to hexahydrodesmethoxygelsedine, $C_{18}H_{28}O_2N_2$. The loss of the O-methyl was not a simple hydrolysis since the analysis indicated the loss of

the oxygen as well. Hexahydrodesmethoxygelsedine showed no absorption above $240\text{ m}\mu$ in the ultraviolet. Its infrared absorption spectrum contained only one peak in the NH,OH region due to the secondary nitrogen and one in the carbonyl region, but none corresponding to a benzene ring so it was this ring which was hydrogenated.

Reduction of gelsedine with lithium aluminum hydride furnished a mixture from which one product was separated by distillation *in vacuo*. This product of uncertain purity (see experimental part) had lost two oxygens, no longer contained a methoxyl, and its infrared spectrum showed no absorption in the carbonyl region, and only one peak in the OH, NH region. The ultraviolet spectrum of the product of this reduction (Fig. 7) had maxima at $243\text{ m}\mu$ and

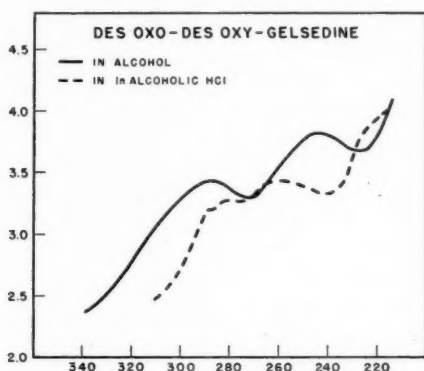


FIG. 7. Ultraviolet spectra of des-oxo-des-oxygelsedine.

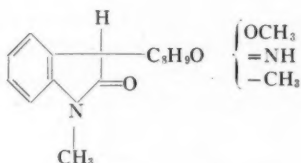
$289\text{ m}\mu$ and minima at $226\text{ m}\mu$ and $277\text{ m}\mu$. The hypsochromic displacement in acid medium (Fig. 7) is characteristic of compounds containing an imino group attached to a chromophoric system.

Of the two nitrogens in gelsedine, one, $\text{N}(b)$ is basic ($\text{pK} \sim 9.3$) and secondary while the other, $\text{N}(a)$ is neutral and tertiary and likely carries the N -methyl group. The latter is contained in a lactam group and is attached to the aromatic ring as is shown by the ultraviolet spectrum of the lithium aluminum hydride reduction product. The carbonyl peak at 1720 cm^{-1} (see gelsevirine) in the infrared and the ultraviolet spectrum of gelsedine are characteristic of oxindoles. A comparative study of the ultraviolet spectra of variously substituted oxindoles (forthcoming publication) suggested that the changes in the ultraviolet absorption in alkaline solution as observed with gelsedine may be indicative of a 1,3-disubstituted oxindole.³ The benzene ring in gelsedine seems to be ortho-disubstituted as indicated by a band at ca. 750 cm^{-1} in its infrared spectrum and in those of its derivatives. Such a band is also present in the infrared spectra of gelsemine and its corresponding derivatives. The

³ From the interpretation of the ultraviolet spectrum Janot, Goutarel, and Friedrich (5) had already proposed an oxindole structure for their base $\text{C}_{19}\text{H}_{24}\text{O}_3\text{N}_2$ which they had assumed to be gelsemicine.

catalytic hydrogenation confirms the presence of a benzene ring and shows the absence of other readily reducible double bonds. It is not likely that the methoxyl is attached to the benzene ring since it is lost during both types of reduction.

From the foregoing the following partial formula for gelsedine can therefore be suggested.



The methoxyl which is lost during the reduction of gelsedine with lithium aluminum hydride or with hydrogen over Adams' catalyst must be in an activated position. Since only one carbonyl appears to be present it is suggested that the methoxyl is in an α - or β -position to the lactam carbonyl and to the benzene ring. That a methoxy group in a benzyl position is removed under the above mentioned conditions is a known fact. But there have been cases observed where a methoxyl in β -position to a carbonyl is lost on hydrogenation over Adams' catalyst⁴. The N-methyl-isatin-like ultraviolet spectrum of gelsedine under certain conditions might be explained by the formation of either a β -methylene oxindole system by base catalyzed elimination of methanol, or of N-methyl-isatin by oxidative cleavage of the β C-C bond. The third oxygen is unaccounted for as yet and is probably present in an ether linkage since there are rather few C-atoms left to make up the other three rings which gelsedine must contain.

Gelsemicine ($C_{29}H_{26}O_4N_2$) contained two methoxyls, one N-methyl, one C-methyl, and one active hydrogen. Its infrared absorption spectrum (curve 3, Fig. 4) showed an NH band, a split band in the carbonyl region, and the usual absorption due to the presence of a benzene ring. The spectrum also contains a strong sharp band at 1500 cm^{-1} which is characteristic of gelsemicine and all its derivatives. This band is not present in the spectrum of gelsedine and therefore has some analytical value in handling mixtures of the two alkaloids. The ultraviolet spectrum of gelsemicine (Fig. 3) in alcohol showed the two maxima characteristic of 1,2,3-trisubstituted indoles (compare Raymond-Hamet (8)), although the general shape of the curve was not the same, the minimum being higher than usual, thus causing a flattening of the curve. The spectrum did not change in acidic solution, but in alkaline solution the minimum was displaced towards higher wave lengths (Fig. 3). The ultraviolet absorption spectrum of tetrahydrocarbazole measured under the same conditions does not show this shift. Nevertheless, the similarity of the ultraviolet spectrum of gelsemicine with that of indoles led Raymond-Hamet (7) to suggest an indole structure for the alkaloid.

⁴ Private communication from Dr. O. E. Edwards.

Both acetyl and benzoyl gelsemicine were neutral substances. The infrared absorption spectra of both derivatives showed no absorption in the NH, OH region but both contained one carbonyl band besides that attributable to the substituent (Fig. 6). Neither derivative contained active hydrogen. The ultraviolet spectrum of acetylgelsemicine was the same as that of the alkaloid.

Of the two nitrogens in gelsemicine one is secondary and basic while the other is tertiary and neutral and probably carries the N-methyl group. If the assumption of an indole nucleus be correct (and the evidence is strengthened by a positive Hopkins-Cole test) then the presence of another chromophoric group must be postulated to account for the additional absorption in the ultraviolet causing the flattening of the curve (1) and for the difference in absorption in alkaline solution. The infrared spectrum of the base contains a very intense second peak at 1632 cm^{-1} (curve 3, Fig. 4) similar to that present in the spectra of corynantheine and Py-tetrahydroalstonine (1) and hence the second chromophoric group is likely similar to that of the latter. It is not, however, identical since gelsemicine is not hydrolyzable by acids (94% of the base being recovered on acid hydrolysis of the benzoylated mixture).

Two of the four oxygen atoms in the molecule are present in methoxyl groups. The ultraviolet spectrum of the alkaloid is different from those of 4-, 5-, and 6-methoxyindoles but similar to that of 7-methoxy-2,3-disubstituted indole (actually 8-methoxy-2,3,4,5-tetrahydrocarbazole), although one of the maxima is at $270\text{ m}\mu$ instead of $285\text{ m}\mu$. The absence of an N-methyl substituent in the model compound might account for this difference. It is therefore possible that one of the methoxyl groups might be present in the benzene ring in the similar position.

The assignment of an empirical formula to the third alkaloid, gelsevirine, and the determination of its functional groups proved difficult. Whereas the perchlorate analyzed correctly for $\text{C}_{21}\text{H}_{24}\text{O}_3\text{N}_2$ containing two methoxyls, one N-methyl, but no C-methyl, the analytical figures obtained from the free base and the methiodide did not agree as well, the methoxyl values particularly being low. It appears that the base may have undergone partial decomposition or hydrolysis in the process of its liberation from its perchlorate. The ultraviolet spectrum of gelsevirine perchlorate was very similar to that of gelsedine ($\lambda_{\text{max}}\ 255\text{ m}\mu$, $\lambda_{\text{min}}\ 231\text{ m}\mu$) but did not change either in acidic or alkaline solution. This is characteristic for either 1,3,3-trisubstituted oxindoles (forthcoming communication) or N-acyl-indolines of the strychnine or aspidospermine type. The infrared spectrum of gelsevirine perchlorate (curve 5, Fig. 4) contained a carbonyl band at 1715 cm^{-1} which was in agreement with an oxindole structure since it was too high for a six-membered lactam (strychnine, 1665 cm^{-1} (6)) or an acyl amide (diaboline, 1660 cm^{-1} (2)). The infrared spectrum also contains a relatively strong band at 3120 cm^{-1} . Such a band is present neither in gelsemine perchlorate nor in gelsedine perchlorate and therefore it cannot be due to an NH in the oxindole or the other moiety of the molecule. Since further all three oxygens are accounted for in a carbonyl and two methoxyls, the absorption band cannot be attributed to a hydroxyl and it may be due to CH-stretching.

EXPERIMENTAL⁵

All infrared absorption spectra were taken in nujol mulls with a Perkin-Elmer double-beam spectrophotometer, model 21. All ultraviolet spectra were taken with a Beckman spectrophotometer model DU.

The finely powdered root of *Gelsemium sempervirens* Ait. (22.6 kgm.) was percolated with methanol until all the alkaloids had been removed (test with Mayer's reagent). The methanol was distilled off under reduced pressure at a water bath temperature of 40–50°. To the residual thick sirup, water was added and the distillation resumed in order to remove the methanol quantitatively. While still warm the tarry residue was poured into a large jar and the distillation flask rinsed with a suspension of filtercel in water. Filtercel (Johns-Manville Hyflo super-cel, 3.7 kgm.) and water (5 l.) were added to the tar and the resulting paste stirred for 24 hr. The contents of the jar was filtered onto a large Buchner funnel and the cake of filtercel and tar was stirred with water (5 l.) another 24 hr. and filtered. This procedure was carried out six more times with 10% acetic acid instead of water, which proved sufficient to complete the extraction of the alkaloids from the tar (test with Mayer's reagent). The filtrates were combined and worked up in suitable portions. It was first extracted three times with ether (extract A), then it was made alkaline with ammonia and extracted with 90:10 ether-methanol until no more alkaloids were taken up by the organic phase (extract V) and finally concentrated aqueous sodium hydroxide was added and the liquor extracted exhaustively with chloroform (extract C).

Extract A did not contain any alkaloids and was discarded.

From the chloroform extract C, the alkaloids were removed by shaking with 10% acetic acid. The combined acid extract was heated to boiling and a concentrated aqueous solution of ammonium nitrate was added. Sempervirine nitrate precipitated as very fine yellow needles. The mixture was cooled, allowed to stand four hours at 0°, and filtered. Yield, 41 gm. The nonprecipitated alkaloids were recovered from the filtrate and combined with extract B.

Extract B in ether solution was shaken repeatedly with normal hydrochloric acid. The combined acid solution was made alkaline with ammonia and extracted with chloroform. The combined chloroform extract was dried over potassium carbonate and the solvent removed by distillation under reduced pressure. The residue was dissolved in acetone and the solution on standing deposited gelsemine in needles having a slight yellow cast. Yield, 58 gm. The acetone mother liquor was evaporated to dryness, the residue (ca. 30 gm.) dissolved in absolute ethanol, and the residual gelsemine removed quantitatively according to Chou's procedure (3).

The dark brown mother liquor from the gelsemine hydrobromide was evaporated to dryness, the residue taken up in water, and the solution filtered through filtercel to remove some insoluble material. The filtrate was made alkaline with ammonia and extracted exhaustively with ether. The combined ether extract was shaken with several portions of 2 N hydrochloric acid, the

⁵ All melting points are corrected.

combined solution was made alkaline with ammonia, and the bases extracted with chloroform (the combined extract contained 200 ml. of chloroform).

For the separation of the minor alkaloids two methods were applied, i.e., benzoylation and acetylation. The former has the advantage of giving a product which crystallizes readily and can be purified more easily than the acetylation product. Both methods, however, give about the same yields.

Benzoylation⁶

The above chloroform extract (200 ml.) together with 10% aqueous sodium hydroxide (700 ml.) and benzoyl chloride (30 ml.) was shaken in a separatory funnel for 10 min. A further 20 ml. of benzoyl chloride was added and the shaking continued until the odor of benzoyl chloride had disappeared (20 min.). The chloroform layer was separated and washed twice with 10% aqueous sodium hydroxide (discarded), five times with 2 *N* sulphuric acid, and three times with water. The acid and water washings which contained the tertiary alkaloids were combined (solution T).

The chloroform solution was then dried and evaporated to dryness leaving a semisolid brown mass (56 gm.) which was dissolved in 250 ml. of benzene. This solution was chromatographed on aluminum oxide No. III (Brockmann scale). A volume of 90 ml. of the solution was poured onto a column containing 300 gm. of alumina. The product was eluted with: (1) benzene (250 ml.), discarded; (2) benzene (250 ml.) which yielded 3.2 gm. of oil; (3) benzene (250 ml.) which gave 0.745 gm. of foam; (4) benzene (250 ml.) which gave 0.482 gm. of foam; (5) benzene (500 ml.) which gave 0.436 gm. of foam; (6) benzene (1000 ml.) which gave 0.400 gm. of oil; (7) benzene-chloroform, 4:1 (500 ml.) which gave 0.139 gm. of oil; (8) benzene-chloroform, 1:1 (500 ml.) which gave 0.088 gm. of oil.

Fraction 2 was triturated with 1:1 ether-pentane in order to remove color and oily material. On filtration of the mixture there was obtained 1.2 gm. of crystalline benzoylated product. Fractions 2, 3 and 4 crystallized on addition of ethanol; 4, 5 and 6 crystallized after standing for several days in alcoholic solution, while 7 and 8 failed to furnish any crystalline material. After recrystallization the benzoylated product (2.40 gm.) melted at 233–240°. The remainder of the benzene solution of the benzoylated product was chromatographed in the same way and the over-all yield from both chromatograms was 8.06 gm. The mother liquor from the crystallizations was rechromatographed and it yielded a further 0.55 gm. of crystalline product. A small sample after three recrystallizations from ethanol still melted at 236–239°. It was dried for eight hours, over phosphorus pentoxide at 100° at 0.1 mm. Found: C, 71.95, 71.67, 71.86, 71.87; H, 6.44, 6.77, 6.37, 6.98; N, 6.31, 6.28. Calc. for $C_{27}H_{30}O_5N_2$: C, 70.11; H, 6.54; N, 6.06. Calc. for $C_{26}H_{28}O_4N_2$: C, 72.20; H, 6.53; N, 6.48%.

Rechromatography of 205 mgm. of the benzoylated product gave three fractions respectively melting at 243–246°, 237–239°, and 234–237°. The infra-

⁶ This method was not applied to the batch of alkaloids obtained by the above described method, but to one worked up by the method previously extant. The yields given here are therefore too low. Improved yields of minor alkaloids are given under "Acetylation Method".

red absorption spectra of these fractions, however, showed that all three were still mixtures of the same components, but in different ratios.

A quantity of the benzoyl compound was hydrolyzed and the resulting mixture of bases crystallized from ethyl acetate, m.p. 136–139°, $[\alpha]_D^{25} -150^\circ$ (*c*, 1.29 in chloroform). Fractional crystallization did not raise the melting point although two forms of crystals were distinctly visible. A few crystals of one form picked out mechanically melted at 160–166°. Chromatography of the mixed bases on alumina did not prove satisfactory as some decomposition occurred.

A small quantity of the crystalline mixed bases was converted to the perchlorate. The crystalline salt was recrystallized three times from methanol-water (1:1). The yield of salt was low, but the mother liquor failed to yield more crystalline salt (see below).

Hydrolysis of the Benzoyl Compound

The benzoyl compound (3.5 gm.) was refluxed for four hours with ethanol containing sulphuric acid (5 *N* in alcohol-water, 7:3) (260 ml.). Water (400 ml.) was then added and after distillation of 300 ml. under reduced pressure, the resulting solution was cooled and extracted with ether (this extract yielded a small quantity of unchanged benzoyl compound). To the acid aqueous liquor ammonia was added to pH ~ 9 , and the solution extracted with five portions of ether⁷. This procedure ensured quantitative removal of the bases. The combined ether extract was washed with water and without drying evaporated to dryness *in vacuo*. The residual amorphous bases weighed 2.46 gm. (92% yield).

Separation of the Bases into Alkaloids A and B

The base mixture (2.40 gm.) obtained on hydrolysis of the benzoyl compound was dissolved in 10% acetic acid (50 ml.), sodium acetate was added, and the solution was seeded with a trace of the crystalline perchlorate described above. Perchloric acid was then added slowly and the turbidity which appeared was cleared as crystals formed on shaking. When a further quantity of 1 ml. of acid failed to cause any turbidity, the mixture was slowly cooled to 0° and the oil which separated solidified on shaking. After 30 min. at 0° the semicrystalline mass was filtered, dried at room temperature, and weighed. It was heated with methanol (1 ml. for every 300 mgm. of perchlorate) until it had all dissolved and an equal volume of water was added. On cooling, crystals separated which were recrystallized from the same mixture to constant melting point. Each mother liquor was worked up as follows: it was distilled under reduced pressure in order to remove the methanol, the residual liquor diluted with water, made alkaline with ammonia, and extracted repeatedly with ether. The combined ether extract after being washed with water was evaporated to dryness without drying and the residual base crystallized from acetone.

All the fractions of base recovered from the perchlorate mother liquors melting above 160° were identical and will be referred to as alkaloid A. The

⁷ Neither ammonia nor sodium hydroxide caused the precipitation of a base. If the solution was made basic with sodium hydroxide, extraction of the base was extremely slow and still incomplete after 10 extractions.

lower melting fractions were still mixtures and were combined with the next lot of mixed bases to be separated. Table I shows the detail of one series of fractional recrystallizations.

A quantity of crystalline perchlorate (1.175 gm.) was decomposed by shaking with ammonia and ether. The ether solution was washed with water, evapor-

TABLE I
FRACTIONAL RECRYSTALLIZATION OF THE PERCHLORATES

| Times recryst. | Base HClO ₄ cryst. | | Base HClO ₄ in solution*, gm. | Free base from soluble perchlorate | | | | |
|-------------------|-------------------------------|------|--|------------------------------------|-------------------|-----------|--------------------|--------|
| | Gm. | M.p. | | Theoretical yield, gm. | Yield, first crop | | Yield, second crop | |
| | | | | | Gm. | M.p. | Gm. | M.p. |
| 0 | — | — | | 2.46 | — | 136–39° | — | — |
| 1 | 2.828 | 151° | 0.502 | 0.350 | 0.270 | 168–70° | 0.039 | 164–7° |
| 2 | 1.976 | 165° | 0.852 | 0.664 | 0.449 | 168.5–70° | 0.051 | 163–6° |
| 3 | 1.557 | 172° | 0.419 | 0.340 | 0.227 | 167–70° | 0.064 | 165–8° |
| 4 | 1.376 | 176° | 0.181 | 0.141 | 0.068 | 165–8° | 0.020 | 153–7° |
| 5 | 1.293 | 181° | 0.083 | 0.065 | 0.040 | 155–8° | — | — |
| 6 | 1.226 | 183° | 0.068 | 0.053 | 0.028 | 136–44° | — | — |

* Calculated as the difference.

ated to dryness, and the residual base crystallized from ethyl acetate, wt. 0.797 gm., m.p. 171–173°.

From 2.46 gm. of mixed bases the foregoing method of separation gave 1.193 gm. of alkaloid A (from the perchlorate mother liquors) and 0.797 gm. of alkaloid B (liberated from the crystalline perchlorate). Unseparated bases and amorphous material recovered from the final mother liquor amounted to 0.367 gm. Hence 81% of the mixture was separated into pure alkaloids.

Identity of Alkaloid A with Gelsemicine

The higher melting fraction of alkaloid A was recrystallized twice from acetone from which it separated in large stout rhombs (Fig. 1), without solvent of crystallization, m.p. 171–172°, $[\alpha]_D^{25} -142^\circ$ (*c*, 0.945 in chloroform). A sample for analysis was dried three hours at 100° at 0.2 mm. Found: C, 66.84, 66.89, 67.27; H, 6.92, 7.00, 7.31; N, 7.78; OCH_3 , 16.22, 16.47, 18.53; $\text{N} \cdot \text{CH}_3$, 2.47, 3.96; $\text{C} \cdot \text{CH}_3$, 3.34; act. hydrogen (Zerewitinow) 0.22%. Calc. for $\text{C}_{20}\text{H}_{26}\text{O}_4\text{N}_2$: C, 67.02; H, 7.31; N, 7.82; 2 OCH_3 , 17.30; 1 $\text{N} \cdot \text{CH}_3$, 4.18; 1 $\text{C} \cdot \text{CH}_3$, 4.18; 1 act. hydrogen, 0.28%. Calc. for $\text{C}_{20}\text{H}_{24}\text{O}_4\text{N}_2$: C, 67.39; H, 6.79; N, 7.86%. In admixture with alkaloid B (m.p. 172.5–174°) it melted at 136–139° but in admixture with a sample of Chou's gelsemicine (m.p. 164–167°) supplied to us by Dr. Raymond-Hamet, it melted at 168–170°. Both the ultraviolet and infrared absorption spectra of alkaloid A (Fig. 3, and curves 3 and 4, Fig. 4) were identical with the corresponding spectra of Chou's gelsemicine.

Gelsemicine Picrate

Gelsemicine (60 mgm.) was dissolved in ethanol (2 ml.) and a slight excess of picric acid in ethanol was added. On scratching the picrate separated in scalelike square plates. It was recrystallized three times from ethanol and dried

for four hours at 100° at 0.2 mm., m.p. 206–208°. Found: C, 53.49; H, 5.21; N, 11.88. Calc. for $C_{20}H_{26}O_4N_2 \cdot C_6H_5O_7N_3$: C, 53.15; H, 4.98; N, 11.92%.

Benzoyl Gelsemicine

Gelsemicine (100 mgm.) was dissolved in chloroform (10 ml.) and to the solution benzoyl chloride (0.4 ml.) and 2 *N* aqueous sodium hydroxide (10 ml.) were added. After the mixture had been shaken for 10 min., benzoyl chloride (0.2 ml.) was added and the reaction mixture shaken for a further 20 min. after which the odor of benzoyl chloride had disappeared. The chloroform layer was separated, extracted twice with 2 *N* aqueous sodium hydroxide, three times with *N* hydrochloric acid, and three times with water. It was then dried over sodium sulphate and evaporated to dryness. The residue was washed with pentane to remove some remaining benzoyl chloride. Yield, 142 mgm. After three recrystallizations from ethanol, benzoyl gelsemicine melted at 235–236°. $[\alpha]_D^{25} - 107^\circ$ (*c*, 0.97 in chloroform). For analysis a sample was dried at 100° at 0.1 mm. for three hours. Found: C, 70.02; H, 6.50; N, 6.21. Calc. for $C_{27}H_{30}O_5N_2$: C, 70.11; H, 6.54; N, 6.06%.

Acetyl Gelsemicine

A solution of gelsemicine (272 mgm.) in benzene (1.5 ml.) and acetic anhydride (1.0 ml.) was refluxed for three hours. The solution was evaporated under reduced pressure, benzene added, and the solution evaporated again under reduced pressure. This process was repeated several times until the excess acetic anhydride had been removed. The residue was dissolved in ethyl acetate, the solution washed three times with *N* hydrochloric acid, three times with water, dried over sodium sulphate, and evaporated to dryness under reduced pressure. Acetyl gelsemicine thus obtained (wt. 286 mgm.) was still colored even after several recrystallizations from ethyl acetate or ethyl acetate–ether. A quantity (224 mgm.) in benzene solution was filtered through a column of 2.5 gm. of acid-washed alumina No. III (Brockmann scale) and the column eluted with alcohol-free chloroform (50 ml.). The colorless product obtained from the eluate (189 mgm.) after two recrystallizations from ethyl acetate–ether, melted at 174–175°. A sample was dried for analysis for three hours at 100° at 0.1 mm. $[\alpha]_D^{25} - 126^\circ$ (*c*, 0.95 in chloroform). Found: C, 65.66; H, 7.15; N, 6.80; $C \cdot CH_3$, 6.74; no active hydrogen. Calc. for $C_{22}H_{28}O_5N_2$: C, 65.98; H, 7.05; N, 7.00; $2 C \cdot CH_3$, 7.48%.

Alkaloid B (Gelsedine)

Alkaloid B (170 mgm.) was recrystallized twice from ethyl acetate from which it separated as fine elongated rhombs (Fig. 2) without solvent of crystallization, m.p. 172.5–174°. For analysis a sample was dried for three hours at 100° at 0.1 mm. $[\alpha]_D^{25} - 159^\circ$ (*c*, 1.35 in chloroform). Found: C, 69.77, 69.81; 69.69; H, 7.52, 7.36, 7.30; N, 8.57; OCH_3 , 8.73, 9.18; $N \cdot CH_3$, 4.22; $C \cdot CH_3$, 3.04, act. hydrogen (Zerewitinow) 0.32. Calc. for $C_{19}H_{24}O_5N_2$: C, 69.49; H, 7.37; N, 8.53; $1 OCH_3$, 9.43; $1 N \cdot CH_3$, 4.57; $1 C \cdot CH_3$, 4.57, act. hydrogen, 0.304%. The ultraviolet and infrared absorption spectra of this base (Fig. 5.

⁸ On slow heating decomposition begins at about 200°.

and curve 2, Fig. 4) were both different from the corresponding spectra of gelsemicine and of gelsemine. Alkaloid B is therefore distinct from gelsemicine and it is suggested to designate it as gelsedine.

Gelsedine is not soluble in alkali at first but during a few hours it slowly dissolves under development of a bright yellow color. After several days a flocculent precipitate appears and the color starts to fade. This behavior has been studied by taking the ultraviolet spectrum of a solution of gelsedine in 1 *N* sodium hydroxide (alcohol-water 1:1) in intervals. The maxima observed were the following:

| | | | | |
|---------------------|-------|-------|-----|---------|
| $\frac{1}{2}$ hr. | 244 | [282] | — | m μ |
| 1 $\frac{1}{2}$ hr. | 242 | 283 | — | m μ |
| 6 hr. | 240 | 284 | — | m μ |
| 2 days | 240 | 282 | 408 | m μ |
| 2 weeks | below | 285 | 405 | m μ |
| | 230 | | | |

[] = inflexion point

Alkaloid B (Gelsedine) Perchlorate

The crystalline perchlorate (50 mgm.) obtained in the separation of the alkaloids was recrystallized from water-methanol (1:1) m.p. 183°⁹. It was kept overnight over calcium chloride in an evacuated desiccator. $[\alpha]_D^{25}$ -96° (*c*, 0.73 in chloroform). Found: C, 50.98, 51.29, 51.23; H, 6.01, 6.30, 6.27; N, 6.57, 6.14; Cl, 8.10. Calc. for $C_{19}H_{24}O_3N_2 \cdot HClO_4 \cdot H_2O$: C, 51.06; H, 6.06; N, 6.27; Cl, 7.93%; H_2O : 4.03%. For reanalysis a sample of the salt was dried *in vacuo* at 120° to constant weight. Loss on weight: 3.78%. Found C, 53.41; H, 5.78; N, 6.43. Calc. for $C_{19}H_{24}O_3N_2 \cdot HClO_4$: C, 53.21; H, 5.88; N, 6.53%.

Gelsedine Picrate

This was prepared like gelsemicine picrate and recrystallized three times from ethanol, m.p. 224–226° (dec.)¹⁰. For analysis it was dried at 100° at 0.1 mm. for four hours. Found: C, 54.03; H, 4.84; N, 12.37. Calc. for $C_{19}H_{24}O_3N_2 \cdot C_6H_3O_7N_3$: C, 53.86; H, 4.88; N, 12.56%. In order to observe a melting point depression on admixture with gelsemicine picrate, unusually long grinding in a mortar was necessary (m.p. 191–195°). Ordinary mixing gave m.p. 198–207°.

Benzoyl Gelsedine

This was prepared as described for the similar derivative of gelsemicine. After three recrystallizations from ethanol it melted at 251–252°. In admixture with benzoyl gelsemicine, m.p. 235–236°. A sample for analysis was dried at 100° at 0.2 mm. for four hours. $[\alpha]_D^{25}$ -116° (*c*, 0.99 in chloroform). Found: C, 72.23; H, 6.55; N, 6.54; act. hydrogen (Zerewitinow) nil. Calc. for $C_{26}H_{28}O_4N_2$: C, 72.20; H, 6.53; N, 6.48%.

Acetyl Gelsedine

The method described for the preparation of acetyl gelsemicine gave with gelsedine an impure product which did not crystallize well. The required derivative was prepared as follows. A mixture of gelsedine (75 mgm.), pyridine

⁹ With very slow heating water is given off between 150°–160° and at 183°, and the partially melted substance melts completely at 204°.

¹⁰ On slow heating decomposition starts at ca. 218°.

(1 ml.), and acetic anhydride (0.5 ml.) was allowed to stand at room temperature for 24 hr. Pyridine and acetic anhydride were removed by evaporating the mixture several times with benzene. The residue was dissolved in ethyl acetate, the solution washed six times with water, dried over sodium sulphate, and evaporated to dryness. The residue was crystallized twice from ethyl acetate, m.p. 165–166°. In admixture with acetyl gelsemicine, m.p. 148–152°. For analysis the product was dried at 100° at 0.1 mm. for three hours. $[\alpha]_D^{25} -139^\circ$ (c, 0.72 in chloroform). Found: C, 67.99; H, 7.43; N, 7.42. Calc. for $C_{21}H_{26}O_4N_2$: C, 68.09; H, 7.07; N, 7.56%.

Hydrogenation of Gelsedine

Gelsedine (100 mgm.) in glacial acetic acid and 30 mgm. of Adams' catalyst were shaken in a hydrogen atmosphere. The hydrogen uptake stopped as soon as all the platinum oxide had been reduced. No hydrogen was taken up during the next three hours. The hydrogenation, therefore, was continued at 60–70°. The hydrogen absorption was very slow. After eight hours another 20 mgm. of Adams' catalyst was added and the hydrogenation continued for another eight hours. After cooling the solution was filtered and the acetic acid removed under reduced pressure. The residue was taken up in water, made alkaline with ammonia, and extracted with ether. Large quantities of ether were necessary because the base was only sparingly soluble in this solvent. The combined ether extract was dried over potassium carbonate. During the evaporation of the solvent silky white needles separated. They were very soluble in methanol and ethanol and almost insoluble in ether, ethyl acetate, and acetone. For analysis they were recrystallized twice from ethanol–acetone and dried for three hours at 0.05 mm. and 100°, m.p. 277°. Found: C, 71.15, 71.24; H, 9.13, 9.00; OCH_3 , 0.0. Calc. for $C_{18}H_{28}O_2N_2$: C, 71.01; H, 9.27%.

The ultraviolet spectrum of this hexahydrodesmethoxygelsedine did not show any absorption above 240 m μ .

Reduction of Gelsedine with Lithium Aluminum Hydride

A solution of 150 mgm. of gelsedine in 20 ml. of dry ether was slowly added to an emulsion of 300 mgm. of lithium aluminum hydride in 10 ml. of dry ether. The mixture was refluxed for three hours, and the excess lithium aluminum hydride destroyed by addition of 6 ml. of methanol. After boiling for another hour the mixture was filtered through filtercel. The filtered precipitate was washed with chloroform, and the combined filtrates washed with water (four times), dried over potassium carbonate, and evaporated to dryness. Yield: 138 mgm. The oily material could not be obtained crystalline from any of the usual solvents. Therefore, it was distilled at 2×10^{-4} mm. and 130–150° in a metal block. The oil crystallized partly after standing at room temperature for several weeks. It was analyzed in this state. Found: C, 76.55; H, 8.93; N, 9.21; OCH_3 , 0.0. $C_{19}H_{26}ON_2$: C, 76.47; H, 8.78; N, 9.39. The infrared spectrum showed no band in the carbonyl region.

The Acetylation Method

The crude basic mixture from 22.6 kgm. of root obtained before benzylation (see above) was added to dry benzene (100 ml.) containing acetic anhydride

(70 ml.) and the solution refluxed for 3.5 hr. The excess acetic anhydride was removed by evaporating several times with benzene and the final dry residue (30 gm.) was dissolved in ethyl acetate. The solution was washed three times with 2 *N* sodium carbonate (discarded), four times with 2 *N* hydrochloric acid, and three times with water. The acid and aqueous washings which contained the tertiary bases were combined (solution T). The washed ethyl acetate solution was dried over sodium sulphate and evaporated to dryness under reduced pressure. The residue (wt. 20 gm.) was dissolved in benzene (250 ml.) and worked up in two batches.

The first batch (150 ml. of the solution) was chromatographed on a column containing 150 gm. of acid washed alumina No. III (Brockmann scale). The elution gave the following fractions: (1) trace from 100 ml. of benzene; (2) dark red, 9.061 gm. from 150 ml. benzene; (3) orange, 0.917 gm. from 250 ml. benzene; (4) yellow, 0.480 gm. from 375 ml. chloroform; (5) yellow, 1.050 gm. from 250 ml. chloroform; (6) brown, 1.088 gm. from 250 ml. chloroform containing 0.75% ethanol. Fractions 1 and 6 were discarded. Fractions 3, 4, and 5 when combined and crystallized from ethyl acetate - ether yielded 1.855 gm. of acetyl product. Fraction 2 contained several red pigments which were very difficult to remove. When dissolved in ethyl acetate - ether, the solution on standing 24 hr. deposited 2.861 gm. of dark brown crystalline material. This was rechromatographed on 60 gm. of alumina. The pigments were eluted first by benzene while the middle fractions (benzene, benzene-chloroform, chloroform containing 0.75% ethanol) gave 1.959 gm. of almost colorless crystals.

All the mother liquors from the crystallizations were combined, evaporated, and the residue rechromatographed in benzene solution on alumina. Most of the pigments were eluted first while the subsequent fractions of the eluate yielded 2.45 gm. of crystalline acetyl product. The over-all yield from 22.6 kgm. of bark was 9.3 gm. (corresponds to ca. 12 gm. of benzoyl product).

Alkaloid C (Gelsevirine)

Solution T (see above) contained the nonacetylated (or nonbenzoylated bases) as sulphates. Addition of perchloric acid to the solution caused the gradual separation of an oil. After standing for three months the oil was covered with a crystalline perchlorate which was loosened with a spatula and separated from the very viscous oil and the aqueous liquor by decantation. The crystals (wt. 1.9 gm.) were dissolved in methanol and the solution allowed to stand at room temperature for two months. After that time a rather pure perchlorate (alkaloid C perchlorate) had separated which was filtered. After standing another month the mother liquor deposited a second crop. Several crops of crystals were thus slowly obtained. The oil from which the perchlorate had first been separated was dissolved in methanol and the solution after standing three months at room temperature had deposited 200 mgm. of the same perchlorate. So far, about 1 gm. of this perchlorate has been isolated.

A quantity of the perchlorate (200 mgm.) was recrystallized three times from methanol. It then melted at 250-252°. It did not contain solvent of

crystallization. For analysis a sample was dried at 100° at 0.05 mm. for three hours. Found: C, 55.75; 55.90; H, 5.66, 5.69; N, 6.34; Cl, 8.15; OCH₃, 13.95; NCH₃, 3.10; C·CH₃, 0.0. Calc. for C₂₁H₂₄O₃N₂·HClO₄: C, 55.69; H, 5.56; N, 6.19; Cl, 7.83; 2OCH₃, 13.72; N·CH₃, 3.32. Calc. for C₂₁H₂₆O₃N₂·HClO₄: C, 55.44; H, 5.96; N, 6.16; 2OCH₃, 13.62; NCH₃, 3.30%.

Gelsevirine

The base liberated from the perchlorate could not be crystallized. It was distilled at 130–150° at 10⁻⁴ mm., and the colorless oil thus obtained analyzed. Found: C, 71.18; H, 7.00. Calc. for C₂₁H₂₄O₃N₂: C, 71.57; H, 6.87. Calc. for C₂₁H₂₆O₃N₂: C, 71.16; H, 7.39%. The picrate of the base was also an oil.

Gelsevirine Methiodide

The methiodide obtained by adding excess methyl iodide to a solution of the base in acetone was recrystallized three times from ethanol from which it separated as colorless needles, m.p. 259–261°. After drying for three hours at 100° at 0.05 mm. it yielded the following analytical figures. Found: C, 52.08, 52.09, 52.58; H, 5.95, 5.77, 6.05; N, 5.48, 5.43; OCH₃, 7.69, 8.40; N·CH₃, 6.28. Calc. for C₂₁H₂₄O₃N₂·CH₃I· $\frac{3}{2}$ H₂O: C, 52.02; H, 5.65; N, 5.52; H₂O, 2.6. Calc. for C₂₁H₂₆O₃N₂·CH₃I· $\frac{1}{2}$ H₂O: C, 52.28; H, 5.98; N, 5.54; H₂O, 1.8; OCH₃, 6.13; NCH₃, 2.96%. Dried at 140° and 0.05 mm. overnight. Loss 1.6%. Found: C, 53.02, 52.87, 52.69; H, 6.07, 6.09, 5.74; N, 5.75. Calc. for C₂₁H₂₄O₃N₂·CH₃I: C, 53.44; H, 5.48; N, 5.67. C₂₁H₂₆O₃N₂·CH₃I: C, 53.22; H, 5.89; N, 5.64%.

To the solution T from which the crystalline and the oily perchlorates had been separated more perchloric acid was added. After standing for about two months a second crystalline perchlorate (about 1.5 gm.) had separated. It was filtered off and dissolved in methanol in which it turned to an oil before going into solution. Crystals have not been obtained from this solution as yet, even after seeding with some crystals of the perchlorate of gelsevirine.

The filtered solution T still contained alkaloids as a heavy precipitate with Mayer's reagent indicated. These alkaloids presumably form very soluble perchlorates.

ACKNOWLEDGMENT

The authors express their gratitude to Dr. Raymond-Hamet, Paris, for the gift of a sample of gelsemicine, to Mr. R. Lauzon and Dr. R. Norman Jones of these laboratories for taking the infrared absorption spectra, to Dr. N. F. H. Bright who made the photomicrographs, and finally to Mr. M. Lesage for technical aid in working up the alkaloid extracts.

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ORGANIC PHOSPHORUS COMPOUNDS

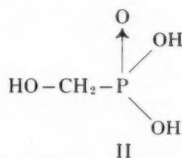
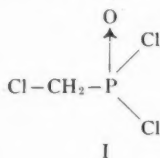
II. PREPARATION OF CHLOROMETHANEPHOSPHONYL DICHLORIDE¹

By R. A. B. BANNARD, J. R. GILPIN, G. R. VAVASOUR,
AND A. F. MCKAY

ABSTRACT

Hydroxymethanephosphonic acid was prepared by treating paraformaldehyde with phosphorus trichloride at atmospheric pressure and subsequent hydrolysis of the resultant complex. Chloromethanephosphonyl dichloride was obtained by chlorination of hydroxymethanephosphonic acid with thionyl chloride in the presence of pyridine. On the other hand hydroxymethanephosphonic acid combined slowly with phosphorus pentachloride to give the hitherto unknown dichlorophosphorylmethanephosphonyl dichloride, $\text{Cl}_2\text{P}(\text{O})\text{OCH}_2\text{P}(\text{O})\text{Cl}_2$, together with chloromethanephosphonyl dichloride. The structure of dichlorophosphorylmethanephosphonyl dichloride was confirmed by its conversion with phosphorus pentachloride at 78°C . into chloromethanephosphonyl dichloride and phosphorus oxychloride. The preparation of chloromethanephosphonyl dichloride by interaction of paraformaldehyde and phosphorus trichloride in an autoclave at 250°C . was studied in reference to the influence of heating time on the yield.

Prat, Bourgeois, and Ragon (9) first prepared chloromethanephosphonyl dichloride (I) in 1948 from phosphorus pentachloride and hydroxymethanephosphonic acid (II). Later Yakubovitch, Ginsburg, and Makarov (11) obtained the same compound by the reaction of phosphorus pentachloride with diazomethane, followed by oxidation of the resultant chloromethanephosphonyl dichloride. More recently, Kabachnik and co-workers (3, 4, 5) have prepared this compound by heating a mixture of phosphorus trichloride and paraformaldehyde in an autoclave at 250°C . Prat, Bourgeois, and Ragon (9)



could not obtain chloromethanephosphonyl dichloride by the action of thionyl chloride on hydroxymethanephosphonic acid nor by reaction of phosphorus pentachloride with the hydroxy acid in carbon tetrachloride suspension. The chlorination of hydroxymethanephosphonic acid was reinvestigated using phosphorus pentachloride and thionyl chloride to establish whether yields superior to those (60–65%) reported by Kabachnik and Shepeleva (5) could be obtained.

Hydroxymethanephosphonic acid (II) was obtained as a liquid when Page's (8) procedure was followed. However, the modifications described in the Experimental section gave good yields of crystalline acid II. Crude hydroxymethanephosphonic acid has a melting point of $84\text{--}86^\circ\text{C}$. in a closed

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tube and it is not contaminated with nonionizable chlorine as Prat and co-workers (9) claimed. Recrystallization of this crude acid from ethanol-ethyl acetate raised the melting point to 98.5–100.5°C. as reported previously by Kabachnik and Shepeleva (5). Hydroxymethanephosphonic acid melting at 98.5–100.5°C. appears to be much less hygroscopic than the material melting at 88–90°C., which suggests that the acid having the lower melting point contains a small proportion of a very hygroscopic impurity. Microanalysis of both samples, however, gave no indication of the presence of an impurity.

Chlorination of hydroxymethanephosphonic acid with thionyl chloride gave a 56.6% yield of chloromethanephosphonyl dichloride (I).

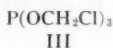
A mixture of phosphorus trichloride and paraformaldehyde heated in a stainless-steel autoclave at 250°C., yielded chloromethanephosphonyl dichloride as previously reported by Kabachnik and co-workers (3, 4, 5). Kabachnik and Shepeleva (5) established that maximum yields of 60–65% were obtained with a molar ratio of phosphorus trichloride to formaldehyde of 1.5:1 and with heating periods of 5 to 10 hr. at 235–250°C. The present studies (cf. Table I) of the effect of heating time on the yield of chloromethanephosphonyl dichloride (I) indicate that maximum yields of 53% are obtained with heating periods of five to six hours. Longer or shorter heating periods cause a marked decrease in yield. Run 2, in which the mixture of phosphorus trichloride and formaldehyde was allowed to stand at room temperature for 17 hr. in the sealed autoclave prior to heating at 250°C., shows that prolonged standing at room temperature has no influence on the yield. However in run 3, where phosphorus pentachloride (0.385 mole) was added to the reaction mixture at room temperature prior to heating, a very marked decrease in yield occurred. In runs 6 and 7, the phosphorus trichloride and paraformaldehyde were combined at atmospheric pressure according to the method of Page (8) for the preparation of hydroxymethanephosphonic acid. The resultant turbid sirup was transferred to the autoclave and heated under the conditions specified in Table I. The abrupt decrease in yield from those obtained in runs 4 and 5, which were performed under otherwise identical conditions, suggests that the hydrogen chloride which is evolved during formation of the phosphorus trichloride-formaldehyde complex is beneficial in the interaction of these substances at

TABLE I
EFFECT OF HEATING TIME ON YIELD OF $\text{ClCH}_2\text{POCl}_2$

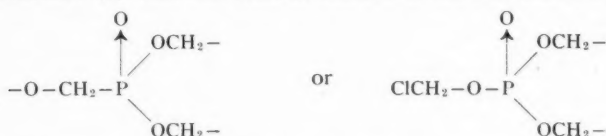
| Run No. | $(\text{CH}_2\text{O})_n$, moles | PCl_3 , moles | Temp., °C. | Gauge pressure, p.s.i. | Heating time, hr. | Yield $\text{ClCH}_2\text{POCl}_2$, moles | % Yield |
|---------|-----------------------------------|------------------------|------------|------------------------|-------------------|--|---------|
| 1 | 0.500 | 0.750 | 245–249 | 330–340 | 1.0 | 0.195 | 39.0 |
| 2 | 0.500 | 0.750 | 250–252 | 335–350 | 1.0 | 0.200 | 40.0 |
| 3 | 0.500 | 0.750 | 249–250 | 400–410 | 1.0 | 0.026 | 5.2 |
| 4 | 0.500 | 0.750 | 249–250 | 330–350 | 3.0 | 0.226 | 45.2 |
| 5 | 1.00 | 1.50 | 249–250 | 365–380 | 3.0 | 0.467 | 46.7 |
| 6 | 1.00 | 1.50 | 247–250 | | 3.0 | 0.328 | 32.8 |
| 7 | 1.00 | 1.50 | 243–250 | 310 | 3.0 | 0.327 | 32.7 |
| 8 | 0.500 | 0.750 | 246–251 | 390–400 | 5.0 | 0.264 | 52.8 |
| 9 | 0.500 | 0.750 | 246–255 | 380–410 | 6.0 | 0.265 | 53.0 |
| 10 | 0.500 | 0.750 | 247–251 | 390–410 | 7.0 | 0.242 | 48.4 |

elevated temperatures and pressures. Kabachnik and Shepeleva (5) infer that there is no difference whether the substances are heated directly in the autoclave or converted to the phosphorus trichloride - formaldehyde complex at atmospheric pressure before heating in the autoclave. However, the low yields in runs 6 and 7 are contrary to this inference.

These authors (5) have discussed the mechanism of this reaction and they have concluded that the tarry residues which remain after removal of the chloromethanephosphonyl dichloride are formed by an intermolecular Arbuzov (1; 6, p. 121) rearrangement of tri(chloromethyl)phosphite (III).

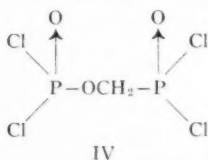


It was assumed (5) that the residue contained the structural elements

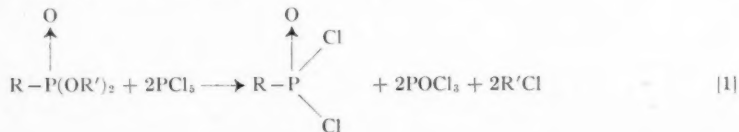


since the residue on heating with phosphorus pentachloride yielded additional chloromethanephosphonyl dichloride by the cleavage of P-O-C bonds. This result agrees with the postulated mechanism for formation of the residue. However, numerous attempts to confirm the production of chloromethanephosphonyl dichloride by heating the residue with phosphorus pentachloride under the conditions given (5) were unsuccessful. It is concluded that either the experimental conditions are not sufficiently specific to follow or the proposed mechanism of formation of the nondistillable residue is inadequate.

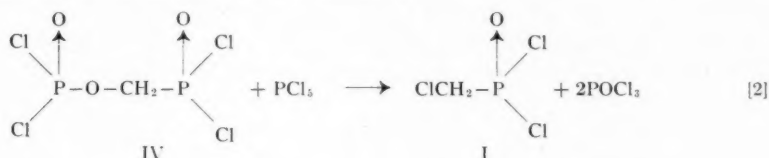
Hydroxymethanephosphonic acid in methylene chloride on treatment with phosphorus pentachloride gave the hitherto unknown dichlorophosphorylmethanephosphonyl dichloride (IV) along with the expected chloromethane-



phosphonyl dichloride. The structure of dichlorophosphorylmethanephosphonyl dichloride (IV) was inferred by its percentage composition and molecular refractivity. This was confirmed by the behavior of the compound on treatment with phosphorus pentachloride. Esters of phosphonic acids, on heating with phosphorus pentachloride, undergo cleavage according to equation [1] (2; 6, p. 62; 10).

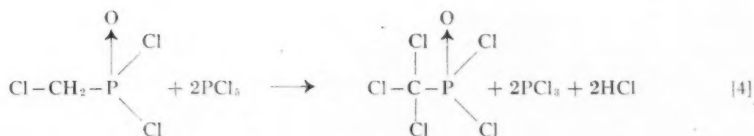
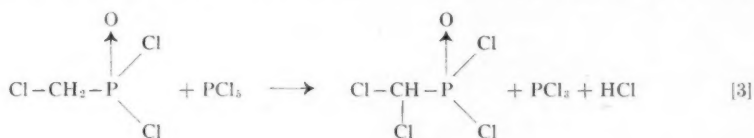


On the basis of reaction [1] dichlorophosphorylmethanephosphonyl dichloride (IV) should be converted to chloromethanephosphonyl dichloride (I) and phosphorus oxychloride as in equation [2].



In agreement with this equation dichlorophosphorylmethanephosphonyl dichloride (IV) heated with an equimolar quantity of phosphorus pentachloride gave a 61% yield of chloromethanephosphonyl dichloride (I) and a 104% yield of phosphorus oxychloride based on unrecovered IV. Hydrogen chloride, phosphorus trichloride, and an unknown crystalline substance (m.p. 175–177°C. with decomposition), which contains phosphorus and chlorine, were obtained as by-products of this reaction (cf. Table II). It is obvious from these results that one or more side-reactions are occurring. The small discrepancy between the quantity of phosphorus oxychloride isolated and that theoretically obtainable via reaction (2) can be explained by the unavoidable partial oxidation of by-product phosphorus trichloride to phosphorus oxychloride (7).

Since a large portion of the dichlorophosphorylmethanephosphonyl dichloride (IV) was recovered unchanged (cf. Table II), it is considered probable that the side-reaction is substitutive chlorination of chloromethanephosphonyl dichloride (I) by phosphorus pentachloride as shown in equations [3] and [4].



Reactions [3] and/or [4] would explain the low yield of the dichloride (I).

Qualitative confirmation of this hypothesis has been obtained by heating chloromethanephosphonyl dichloride (I) with phosphorus pentachloride under the same conditions as used for the cleavage of dichlorophosphorylmethanephosphonyl dichloride (IV). The substances react with evolution of hydrogen chloride producing a solution which contains a large proportion of phosphorus trichloride, a trace of phosphorus oxychloride, unreacted I, and the colorless crystalline substance of m.p. 175–177°C. (with decomposition). All of these

products were isolated from the previously described experiment on the cleavage of IV.

EXPERIMENTAL²

Hydroxymethanephosphonic Acid

One hundred and thirty-seven grams (1.00 mole) of phosphorus trichloride was placed in a 200-ml., four-neck, round-bottom flask equipped with a "trubore" stirrer, thermometer, addition tube, and reflux condenser protected with a calcium chloride tube. Ninety grams (3.00 mole) of paraformaldehyde were added in small portions over a period of 45 min. Each addition was made at 40 to 45°C. and the mixture heated to 60–65°C., at which temperature an exothermic reaction occurred with evolution of hydrogen chloride causing the temperature to rise to 75–78°C. As soon as the temperature began to fall, the solution was cooled to the starting temperature by means of an ice-bath and the cycle repeated. After all the formaldehyde had been added, the opalescent solution was stirred at 80°C. until a colorless solution was obtained (one to two hours). The solution was allowed to stand overnight and the phosphorus trichloride-formaldehyde complex hydrolyzed by pouring the solution into 2 liters of water stirred mechanically at 25°C. At first the oily complex remained immiscible although the temperature rose to 43°C. and formaldehyde was evolved. After the mixture was stirred for 30 min. a clear solution resulted but stirring was continued for a further 30 min. The solution was filtered and concentrated to a volume of about 250 ml. by distillation *in vacuo*. Treatment of the residue as in either Method A or B below produced colorless crystalline hydroxymethanephosphonic acid in 87–92% yield (97.5–102 gm.) m.p. 84–86°C. (closed tube).

Method A.—The pale yellow solution was diluted with 300 ml. of absolute ethanol and about 250 ml. of the ethanol removed by slow distillation at atmospheric pressure, to remove any trace of residual formaldehyde as the diethyl acetal. The residue was concentrated to constant bulk at 0.1 mm. pressure at 80°C. and allowed to cool to room temperature while evacuation was continued. The substance crystallized completely to a very hard colorless solid after one to two hours.

Method B.—The pale yellow solution was concentrated to constant bulk at 0.1 mm. pressure at 80°C. and allowed to cool to room temperature while evacuation was continued. The substance crystallized completely after two hours to two days.

The crude acid (100 gm.) was recrystallized by dissolving it in absolute ethanol (65 ml.) followed by filtration in a dry-box and addition of purified ethyl acetate in 200-ml. portions followed by cooling in the refrigerator to obtain successive crops of crystals, yield 52 gm. (52%). Most of the recrystallized acid had a melting point of 88–90°C. but one crop had a melting point of 98.5–100.5°C. Calc. for $\text{CH}_3\text{O}_4\text{P}$: C, 10.73; H, 4.50; P, 27.67%. Found for acid m.p. 88–90°C.: C, 10.72; H, 4.53; P, 28.15%. Found for acid m.p. 98.5–100.5°C.: C, 11.09; H, 4.88; P, 27.44%.

² All melting points and boiling points are uncorrected. Microanalyses by C. W. Beazley, Skokie, Ill.

Chlorination of Hydroxymethanephosphonic Acid with Thionyl Chloride in the Presence of Pyridine

Hydroxymethanephosphonic acid (22.4 gm.; 0.200 mole) was suspended in 150 ml. of anhydrous benzene in a 500-ml., three-neck, round-bottom flask equipped with a "tribore" stirrer, thermometer, dropping funnel, and reflux condenser protected with a calcium chloride tube. Pyridine, 47.5 gm. (0.600 mole), was added in one portion to the stirred suspension at room temperature, causing the phosphonic acid to change to a sirup which settled to the bottom of the flask. The stirred mixture was heated to 55°C. and purified thionyl chloride (71.4 gm.; 0.600 mole) was added at 55–65°C. over a period of 30 min. Vigorous evolution of sulphur dioxide occurred during the addition and a homogeneous solution resulted. The solution was allowed to cool to 30°C. over a period of two hours while stirring was continued. Pyridine hydrochloride began to separate and the mixture was stirred in an ice-bath for 30 min. to complete precipitation. The crystalline material was collected by suction filtration and washed with 5 × 60 ml. of anhydrous benzene. The filtrate and washings were combined and concentrated by distillation at atmospheric pressure in an apparatus protected from entry of moisture. The residue was fractionated *in vacuo* yielding 18.9 gm. (56.6%) of chloromethanephosphonyl dichloride, b.p. 90–93°C. (18 mm.), $n_D^{24.8}$ 1.4976.

In another experiment using the same quantities of reactants as above and the same procedure, except that the thionyl chloride and pyridine were mixed before addition to the benzene suspension of hydroxy acid, 12.4 gm. (37.1%) of chloromethanephosphonyl dichloride b.p. 77–78°C. (10 mm.), $n_D^{24.8}$ 1.4970, $d_4^{25.0}$ 1.650 were obtained. Kabachnik and Shepeleva (5) report b.p. 77–79°C. (10 mm.), n_D^{20} 1.4978–1.4990, d_4^{20} 1.6361.

Chlorination of Hydroxymethanephosphonic Acid with Phosphorus Pentachloride in Methylene Chloride

Phosphorus pentachloride (187 gm.; 0.900 mole) was suspended in 150 ml. of anhydrous methylene chloride in a 500-ml. three-neck, round-bottom flask equipped with a "tribore" stirrer, addition tube, thermometer, and reflux condenser protected with a calcium chloride tube. Hydroxymethanephosphonic acid, 33.6 gm. (0.300 mole) was placed in a 250 ml. Erlenmeyer flask and attached to the addition tube by means of wide diameter rubber tubing. The hydroxymethanephosphonic acid was added to the stirred suspension of phosphorus pentachloride at 23–26°C. over a period of 30 min., during which vigorous evolution of hydrogen chloride occurred. This mixture was heated under reflux for 18 hr. while slow evolution of hydrogen chloride continued. After heating had been in progress for two hours a homogeneous pale yellow solution resulted. This solution was concentrated by heating at 40 to 60°C. under pressure of 40–60 mm. It was necessary to complete the concentration in three stages to ensure a reasonable recovery of liquid from the unreacted phosphorus pentachloride which separated on cooling the solution. The phosphorus pentachloride was collected by suction filtrations in the dry-box. The final filtrate was transferred to a 50 ml. modified Claisen flask and traces

of volatiles removed by heating to 50°C. in a water bath at 20 mm. pressure. The residue was fractionated *in vacuo* yielding 10.6 gm. (21.1%) of chloromethanephosphonyl dichloride, b.p. 78–81°C. (10 mm.), $n_D^{24.8}$ 1.4978 and 26.7 gm. (33.5%) of dichlorophosphorylmethanephosphonyl dichloride, b.p. 94–95°C. (0.2 mm.), $n_D^{24.8}$ 1.4990, $d_4^{25.5}$ 1.750. Calc. for $\text{CH}_2\text{P}_2\text{O}_3\text{Cl}_4$: C, 4.52; H, 0.76; P, 23.30; Cl, 53.32%. Found: C, 4.78; H, 0.88; P, 22.97; Cl, 52.90%. Molecular refractivity calc.: 44.05. Found: 44.35.

Reaction of Paraformaldehyde with Phosphorus Trichloride at 250°C.

All runs were made in a 300 ml. stainless-steel autoclave equipped with a pressure gauge.

Fifteen gm. (0.500 mole) of paraformaldehyde and 103 gm. (0.750 mole) of phosphorus trichloride were placed in the autoclave which was sealed immediately and shaken thoroughly to ensure mixing. An exothermic reaction occurred. The autoclave was heated to 250°C. over a period of two and one quarter hours and the temperature was held at 246–255°C. for six hours. The pressure rose to 380 p.s.i. during heating to 250°C. and remained at 380–410 p.s.i. during the remainder of the heating period. The autoclave was removed from the bath, allowed to stand for one hour, then immersed in an ice bath for 20 min. There was no residual pressure when the autoclave was opened. The dark mobile solution was filtered to remove a small quantity of gray residue, and transferred to a modified Claisen flask. The excess phosphorus trichloride was removed by distillation at 40–60 mm. pressure, after which the residue was fractionated *in vacuo* yielding 44.2 gm. (52.0%) of crude chloromethanephosphonyl dichloride as a colorless mobile liquid of piercing odor; b.p. 77–95°C. (9 mm.); $n_D^{24.8}$ 1.4953 to 1.4944. During the latter stages of the distillation the residue became very dark and viscous. Refractionation of the crude product gave 39.0 gm. (46.7%) of pure material b.p. 79–81°C. (10 mm.), $n_D^{24.8}$ 1.4954 to 1.4959, $d_4^{25.5}$ 1.655.

Action of Phosphorus Pentachloride on Dichlorophosphorylmethanephosphonyl Dichloride

Dichlorophosphorylmethanephosphonyl dichloride 38.9 gm. (0.146 mole) and 30.4 gm. (0.146 mole) of phosphorus pentachloride were placed in a 125 ml. two-neck, round-bottom flask equipped with a "trubore" stirrer and reflux condenser protected with a calcium chloride tube. The mixture was heated slowly in a mechanically stirred oil bath to 77°C. over a period of 50 min., at which temperature a slow evolution of hydrogen chloride was observed. Heating was continued with mechanical stirring at 74–78°C. for a further two and one-quarter hours, during which slow evolution of hydrogen chloride continued. The phosphorus pentachloride had dissolved after heating at 74–78°C. for one hour. This solution was allowed to stand overnight at room temperature, during which a small quantity of phosphorus pentachloride separated. The solution was fractionated yielding the fractions given in Table II.

TABLE II

PRODUCTS FROM REACTION OF DICHLOROPHOSPHORYLMETHANEPHOSPHONYL DICHLORIDE WITH PHOSPHORUS PENTACHLORIDE

| Fraction No. | B.p., °C. | Pressure, mm. | Refractive index, $n_D^{24.8}$ | Density, d_4^t | Wt., gm. | Identity | Moles | % Yield based on equation [2] |
|--------------|-----------|---------------|--------------------------------|------------------|----------|--|--------|-------------------------------|
| 1 | 74 | 745 | 1.5023 | 1.554(25.0) | 3.8 | PCl ₃ | 0.0277 | By-product |
| 2 | 105-106 | 745 | 1.4578 | 1.660(27.0) | 28.4 | POCl ₃ | 0.186 | 104 |
| 3 | 62 | 9 | | | 0.3 | Unknown | | By-product |
| 4 | 71 | 8 | 1.4970 | 1.653(27.5) | 9.1 | ClCH ₂ P(O)Cl ₂ | 0.0545 | 61.0 |
| 5 | 103 | 1 | 1.4982 | 1.755(26.5) | 15.1 | Cl ₂ (O)POCH ₂ P(O)Cl ₂ | 0.0367 | Starting material |
| 6* | | | | | 2.0 | | | |
| 7** | | | | | 2.9 | | | |

*Distillation residues.

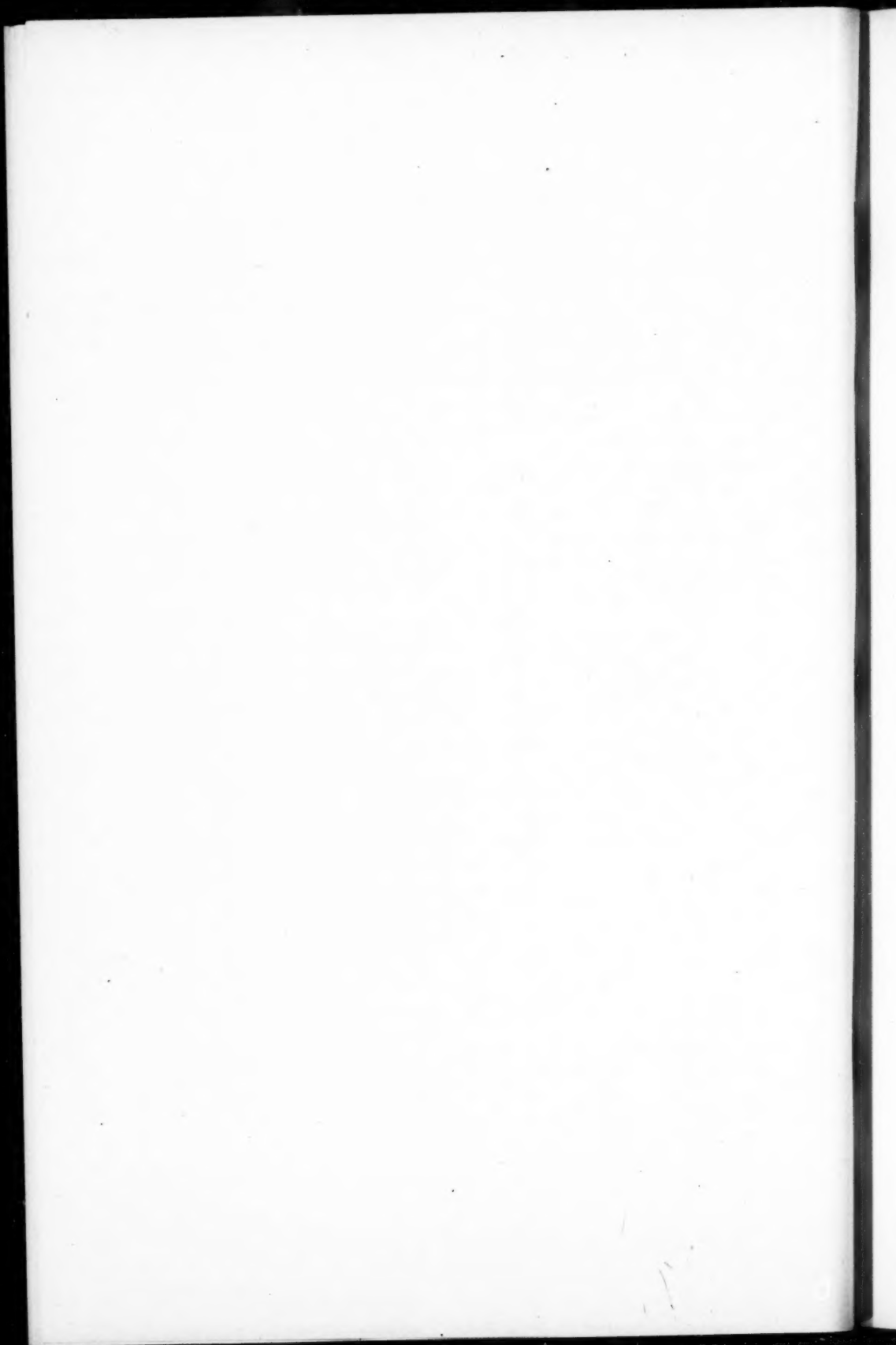
**Transfer losses.

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